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The interplay between nutritional deficiencies and susceptibility to mycotoxicosis: implications for public health and food safety: a review

David Chinonso Anih*, Kayode Adebisi Arowora, Moses Adondua Abah, Kenneth Chinekwu Ugwuoke, Bilyaminu Habibu

Department of Biochemistry, Faculty of Biosciences, Federal University Wukari, Taraba, Nigeria.

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ABSTRACT

Mycotoxins, toxic secondary metabolites produced by fungi, are pervasive contaminants of staple crops, particularly in tropical and subtropical regions. These toxins, including aflatoxins and fumonisins, pose significant health risks, especially in populations suffering from malnutrition. The interplay between nutritional status and susceptibility to mycotoxicosis exacerbates these risks, with nutritional deficiencies impairing the body's ability to detoxify these toxins and vice versa. This manuscript investigates the bidirectional relationship between nutrition and mycotoxin exposure, with a focus on vulnerable populations in resource-limited settings. A systematic review was conducted to explore the interactions between nutritional deficiencies and mycotoxin exposure. A comprehensive search of databases (PubMed, Scopus, Web of Science) yielded peer-reviewed studies published from 2020 to 2025. Inclusion criteria centered on studies examining the relationship between nutritional status and mycotoxin-induced health outcomes. Data were analyzed to assess how protein-energy malnutrition increases susceptibility to mycotoxins and how mycotoxins disrupt nutrient absorption. The review identifies several mechanisms by which heightens the risk of mycotoxicosis, including impaired detoxification processes, immune dysfunction, and nutrient malabsorption. Nutrients such as protein, vitamins A, C, E, and trace elements like zinc and selenium are critical for detoxification and immune defense. Deficiencies in these nutrients, common in mycotoxin-exposed populations, compromise liver function and immune responses, leading to heightened toxicity. Additionally, mycotoxins disrupt intestinal integrity, impairing nutrient absorption and exacerbating malnutrition, creating a toxico-nutritional spiral. This cyclical interaction is most evident in children and pregnant women in low-income regions, where diets are often reliant on mycotoxin-contaminated crops. Addressing the mycotoxin-nutrient interaction requires integrated approaches combining food safety, nutritional interventions, and public health policies. Strategies such as biofortification, micronutrient supplementation, and improved agricultural practices can reduce the burden of mycotoxicosis. Further research into the molecular mechanisms underlying these interactions, along with the development of predictive biomarkers, will aid in creating more effective interventions. Climate-resilient agricultural practices and nutritional strategies are essential for long-term mycotoxin risk reduction

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1. Introduction

1.1. Background on mycotoxins and nutritional vulnerability

Mycotoxins are a diverse group of toxic secondary metabolites produced by fungi such as *Aspergillus*, *Fusarium*, and *Penicillium* (1,2).These toxins commonly contaminate staple crops such as cereals, maize,

*Corresponding author. Tel.:+234 907 823 8896
E-mail address: anih.david@fuwukari.edu.ng

groundnuts, and other nuts, especially under warm and humid conditions typical of tropical and subtropical climates. Such regions often experience both high rates of mycotoxin contamination and widespread nutritional inadequacies, creating an overlapping public health crisis (3).

Among the most studied mycotoxins are aflatoxin B1 and M1, known for their hepatotoxic, immunosuppressive, and carcinogenic effects (3). The risks are further compounded in settings where dietary diversity is limited and food insecurity is common. Evidence shows that children in rural Tanzania, for example, are frequently exposed to both aflatoxins and fumonisins through contaminated staple foods, increasing their risk for growth impairment (4).

Beyond individual-level health effects, mycotoxins impose significant public health and economic burdens. Interventions such as agricultural control programs and food safety policies have shown varying degrees of cost-effectiveness in reducing exposure, but their implementation remains limited in low-income settings (5). Importantly, the overlap between areas of high exposure and high rates of protein-energy malnutrition has drawn attention to a synergistic interaction between mycotoxins and undernutrition that magnifies health risks (6,7).

1.2. Nutritional determinants of host defense

Adequate nutrition is foundational for the body's defense against environmental toxins (6). Key nutrients including protein, vitamins A, C, and E, folate, selenium, and zinc support the immune system and aid in detoxification processes (7). Deficiencies in these nutrients, prevalent in under-resourced settings, compromise host resilience to toxins, including mycotoxins (8).

While the mechanistic roles of these nutrients in hepatic detoxification, immune modulation, and epithelial protection are acknowledged, detailed discussions are provided in the results section (3.1–3.2) to avoid redundancy here.

1.3. Bidirectional interaction between mycotoxins and nutrition

The relationship between nutrition and mycotoxins is not unidirectional. While undernutrition increases susceptibility to mycotoxicosis, mycotoxins themselves can impair nutrient utilization. Experimental and observational data suggest that aflatoxins and fumonisins disrupt nutrient absorption by damaging the intestinal epithelium and downregulating key nutrient transporters (4,8). This can exacerbate existing deficiencies in essential micronutrients and contribute to the persistence of malnutrition.

Interestingly, not all studies have shown a direct linear relationship between mycotoxin exposure and anthropometric deficits. In a cohort study of Nepalese children, aflatoxin exposure during the first 36 months of life was not significantly associated with impaired growth, suggesting that the impact of exposure may depend on contextual factors such as baseline nutritional status, dietary diversity, or co-existing infections (9).

The concept of the toxico-nutritional spirals a cycle in which malnutrition and mycotoxin exposure reinforce each other has been proposed as a model to understand these complex interactions. Populations experiencing food insecurity, especially children and pregnant women, are particularly vulnerable to this spiral due to

their higher metabolic demands and limited access to nutrient-dense foods.

1.4. Rationale and objectives of the review

Mycotoxins continue to pose a significant challenge to food safety and public health, particularly in nutritionally vulnerable populations. With climate change projected to exacerbate fungal proliferation and extend the growing seasons for mycotoxin-producing crops, the global risk of dietary exposure is expected to increase (10). At the same time, genomic advances offer promising tools for predicting and mitigating contamination risks at the source (10).

This review aims to systematically evaluate the interplay between nutritional status and susceptibility to mycotoxicosis, with the following specific objectives:

To explore how malnutrition or nutrient deficiencies increase host vulnerability to mycotoxins;

To examine how mycotoxins, impair nutrient absorption and utilization;

To identify high-risk groups and discuss nutritional strategies for mitigation.

By highlighting this bidirectional relationship, the review seeks to support integrated approaches to food safety, nutrition, and public health policy that can reduce the burden of mycotoxin-related diseases in vulnerable communities.

2. Materials and Methods

This section details the methodology employed to conduct a systematic review on the relationship between nutritional status and susceptibility to mycotoxicosis. A rigorous and structured approach was applied following internationally recognized standards for systematic review conduct and reporting. The process included comprehensive literature searching, transparent inclusion criteria, and critical appraisal using validated tools to ensure methodological integrity. The approach integrates evidence from both randomized and non-randomized studies, ensuring a robust assessment of the interaction between nutrition and dietary mycotoxins.

2.1. Search strategy

A comprehensive search was conducted in PubMed, Scopus, and Web of Science for peer-reviewed studies published between January 2020 and March 2025 (11). This timeframe was selected to align with the release of the PRISMA 2020 guidelines, as well as to capture emerging data related to mycotoxin exposure in the context of climate variability and recent nutritional surveillance updates (12).

2.2. Inclusion and exclusion criteria

Eligible studies were selected based on predefined inclusion and exclusion criteria. To be included, studies had to:

- Be published in peer-reviewed journals between 2020 and 2025,
- Be written in English,
- Investigate the relationship between nutritional status and dietary mycotoxins, and
- Report defined endpoints involving nutrient status, absorption, or physiological responses to mycotoxin exposure.

Studies were excluded if they were editorials, preprints, conference abstracts, animal-only studies without translational relevance, or lacked clear nutritional or toxicological endpoints. These criteria helped streamline the review process and ensure that only studies relevant to the toxico-nutritional interface were analyzed (13).

2.3. Data management and risk of bias assessment

Screening and data extraction were conducted using Rayyan QCRI, a web-based software specifically designed for systematic reviews (14). The initial screening was done independently by two reviewers based on titles and abstracts, followed by full-text assessment for eligibility. Conflicts were resolved by consensus.

To assess the methodological quality of included studies, multiple tools were applied based on study design. For randomized controlled trials, the RoB 2 tool was used to evaluate the risk of bias across five domains (13). For scoping and observational studies, the PRISMA-ScR checklist was applied (15), and guidance from the Cochrane Handbook version 6.3 was followed (16). Literature database combinations were optimized using evidence-based recommendations (17), and academic platform selection followed findings on the retrieval quality of search systems (18). Reporting fidelity of search methods was ensured using PRISMA-S guidelines (19). Non-randomized case series were appraised using the JBI tool (20).

Table 1 summarizes the instruments and guidelines employed throughout the systematic review process, as detailed in Section 2. These include PRISMA 2020 (11) and PRISMA-ScR (15) for reporting, PRESS 2021 (12) for search strategy validation, RoB 2 (13) for bias assessment in RCTs, and the Cochrane Handbook (16) for methodological guidance. The table also includes tools for software-assisted screening (14), database optimization (17), platform suitability (18), search method transparency (19), and appraisal of non-randomized studies (20).

2.4. Study selection flowchart

The study selection process is summarized in Fig. 1, following the PRISMA 2020 format. This includes the number of records identified, screened, excluded (with reasons), and those included in the final synthesis.

3. Outcomes

This section presents the key findings from the literature and offers an integrative discussion on the interactions between nutritional status and mycotoxicosis susceptibility. The discussion is structured around thematic sub-sections reflecting core mechanisms by which nutrient availability modulates host responses to dietary mycotoxins. These include impaired detoxification capacity, immune dysfunction, intestinal malabsorption, and the perpetuation of a toxico-nutritional spiral. Interventions and future research directions are also considered.

3.1. Malnutrition and impaired host detoxification

Nutrient deficiencies particularly of protein, folate, vitamins A, C, E, selenium, iron, and zinc have been consistently shown to impair the liver's capacity to detoxify mycotoxins. The detoxification of xenobiotics, including aflatoxins, primarily involves two critical hepatic enzyme systems: Phase I (cytochrome P450 family) responsible for oxidation, and Phase II (conjugation enzymes like glutathione-S-transferases or GSTs) that facilitate the conversion of toxic intermediates into water-soluble compounds for excretion.

Protein-energy malnutrition directly compromises hepatic enzyme synthesis. Experimental models show that diets deficient in protein significantly reduce hepatic CYP3A4 activity, a key enzyme in aflatoxin B1 biotransformation (21). This reduction impairs the oxidation of aflatoxin B1, leading to prolonged

circulation of the parent toxin and increased cellular damage.

Table 1. Tools used in literature screening and review

Component	Tool/guideline applied	Citation
Review reporting standard	PRISMA 2020	(11)
Search string validation	PRESS 2021 checklist	(12)
Bias assessment in RCTs	RoB 2 tool	(13)
Screening software	Rayyan QCRI	(14)
Observational study evaluation	PRISMA-ScR checklist	(15)
Eligibility and method guidance	Cochrane Handbook v6.3	(16)
Database search optimization	Bramer method for translating and optimizing search strategies	(17)
Academic search platform suitability	Gusenbauer & Haddaway, 2020	(18)
Search method reporting	PRISMA-S statement	(19)
Case series appraisal	JBI critical appraisal tool	(20)

This table outlines the validated tools, guidelines, and platforms used to ensure methodological rigor during the literature screening, bias assessment, and reporting phases of this systematic review. These instruments were selected to align with best practices and enhance transparency in the evidence synthesis process.

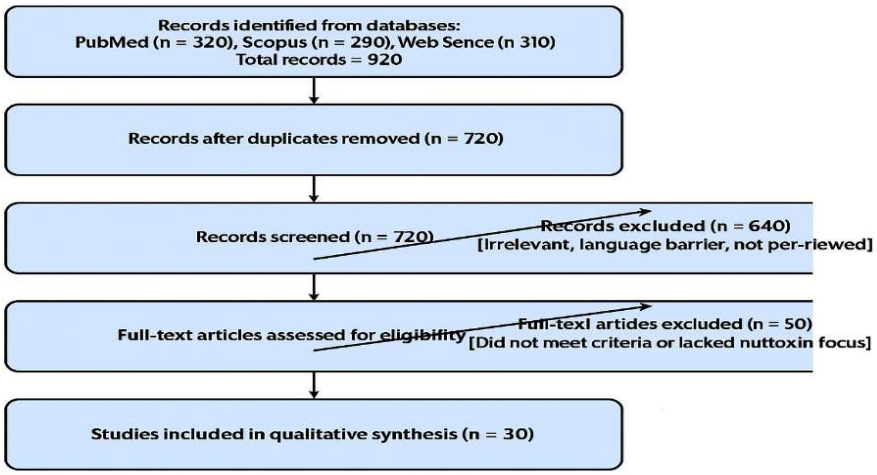

Figure 1. PRISMA flow diagram for study selection on nutritional and mycotoxin-focused research

This PRISMA diagram summarizes the study selection process from 920 identified records to 30 included studies, highlighting exclusions at each stage (11-20). It ensures a transparent and reproducible approach to systematic review.

Selenium, a cofactor of glutathione peroxidases (GPX), plays a crucial antioxidant role in detoxification. Selenium-deficient hepatocytes exposed to fumonisins exhibit heightened oxidative stress and mitochondrial damage, indicating impaired hepatic resilience to mycotoxin insult (22). Similarly, zinc deficiency has been shown to suppress GST expression, weakening Phase II conjugation and thereby compromising toxin elimination (23).

In populations with vitamin E deficiency, particularly malnourished children, studies report exacerbated aflatoxin-induced damage to CYP450 enzymes, further disrupting Phase I detoxification (24). These findings align with broader evidence that low-protein diets not only limit enzyme synthesis but also diminish the availability of essential amino acids required for glutathione production and conjugation reactions (25).

Micronutrient imbalances extend beyond selenium and zinc. Deficiencies in multiple trace elements collectively disrupt conjugation pathways, lowering enzymatic defense against multiple mycotoxins (26). Folate deficiency, for instance, leads to increased DNA adduct formation in the liver when exposed to aflatoxin B1, highlighting the mutagenic risk posed by micronutrient insufficiency (27).

Iron status also modulates detoxification. Iron deficiency anemia has been linked to the downregulation of flavin-containing monooxygenase 3 (FMO3), a lesser-known but critical detoxification enzyme, resulting in slower clearance of mycotoxins from circulation (28). Meanwhile, vitamin C, through epigenetic modulation of CYP2D6, can influence the metabolism of ochratoxin A, with deficiency reducing enzymatic turnover and increasing toxin burden (29).

Recent studies have added further mechanistic insights. Selenium-dependent suppression of GPX1 during malnutrition was shown to heighten deoxynivalenol toxicity in hepatic cells, pointing to the importance of redox regulation in modulating toxin-induced injury (30).

Fig. 2 outlines how deficiencies in protein, selenium, zinc, and vitamins A, C, and E suppress hepatic Phase I enzymes (e.g., CYP3A4, CYP2D6) and inhibit Phase II enzymes (e.g., GST, GPX), leading to impaired conjugation and increased mycotoxin bioaccumulation (21–30). Feedback arrows highlight the regulatory influence of micronutrients on enzyme expression.

3.2. Nutrient deficiencies and immune dysfunction in mycotoxicosis

Nutritional deficiencies compromise the immune system's ability to manage mycotoxin exposure. Table 2 summarizes the immunological consequences of deficiencies in vitamins A, C, D, E, folate, selenium, zinc, and iron.

Rather than repeating individual pathways, this section focuses on synthesizing how these micronutrients collectively disrupt mucosal immunity, cytokine regulation, and barrier integrity factors that heighten vulnerability to dietary mycotoxins. Vitamin A plays a pivotal role in mucosal integrity and secretory IgA responses. Its deficiency weakens gut-associated lymphoid tissue (GALT) and increases intestinal permeability, facilitating greater aflatoxin B1 translocation and reducing local immune responses (31). Zinc deficiency further exacerbates intestinal damage, promoting T-cell apoptosis and reducing lymphocyte viability under fumonisin exposure (32).

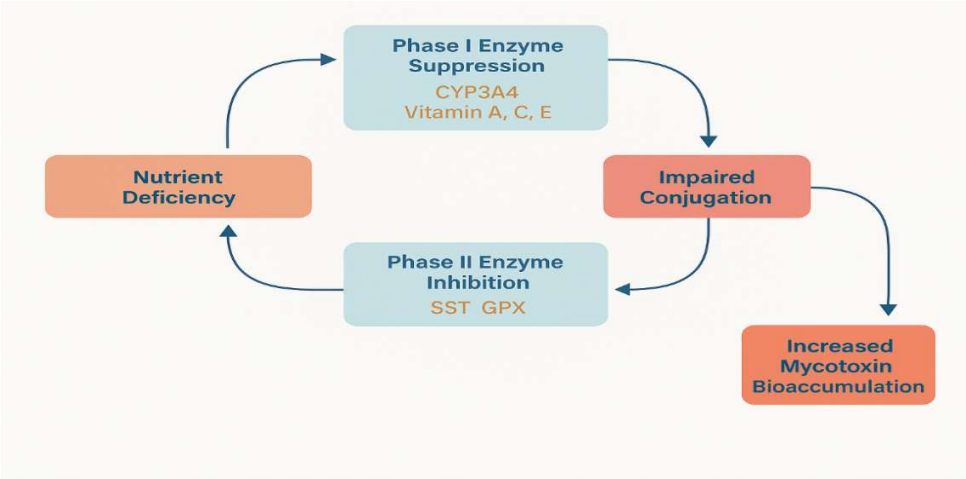

Figure 2. Biochemical pathway of hepatic detoxification impairment under nutrient deficiency

Conceptual illustration based on evidence synthesized from studies (21–30), highlighting how deficiencies in protein, selenium, zinc, and antioxidant vitamins impair Phase I and Phase II detoxification enzymes.

Table 2. Key nutrients influencing susceptibility to mycotoxins

Nutrient	Primary immune function	Deficiency consequence	Citation
Vitamin A	Maintains mucosal surfaces and IgA production	Increases intestinal permeability and aflatoxin uptake	(31)
Zinc	Supports epithelial repair and T-cell function	Promotes barrier breakdown and lymphocyte apoptosis	(32), (36)
Selenium	Cofactor for GPX, enhances NK cell activity	Reduces oxidative defense and innate immunity	(33)
Vitamin D3	Modulates T-helper cell balance	Favors pro-inflammatory Th17 polarization	(34)
Vitamin E	Protects immune cells via Nrf2-regulated antioxidant signaling	Disrupts macrophage function and increases oxidative stress	(35)
Iron	Enables NET formation	Impairs pathogen defense during DON exposure	(37)
Vitamin C	Neutralizes ROS, regulates inflammasome activation	Exacerbates FB1-induced inflammation via NLRP3 activation	(38)
Folate	Essential for methylation, DNA synthesis, cytokine regulation	Aggravates trichothecene-related cytokine dysregulation	(39)
Vitamin A + Zinc	Maintains gut microbiota balance and mucosal immunity	Amplifies gut dysbiosis under aflatoxin exposure	(40)

This table summarizes the specific roles of selected nutrients in maintaining immune competence and the consequences of their deficiencies in the context of mycotoxin exposure.

Selenium, a trace element vital to glutathione peroxidase activity, also influences immune surveillance. In malnourished children exposed to ochratoxin A, selenium supplementation was found to restore natural killer (NK) cell activity, suggesting its relevance in innate immune defense (33). Vitamin D3, though not classically associated with antioxidant protection, was shown to modulate T-helper cell differentiation, and its deficiency skewed immune responses toward a pro-inflammatory Th17 phenotype in mycotoxin-exposed individuals (34).

Vitamin E, a lipid-soluble antioxidant, mitigates oxidative damage in immune cells. Its deficiency disrupts macrophage function, suppresses phagocytic activity, and impairs nuclear factor erythroid 2–related factor 2 (Nrf2) signaling, leading to exaggerated responses to aflatoxin B1 (35). Zinc's role extends beyond T-cell survival to include the regulation of epithelial transporters. Specifically, ZIP1 and ZIP8 downregulation under mycotoxin challenge compromises barrier repair and facilitates antigen penetration into submucosal layers (36).

Iron, essential for neutrophil extracellular trap (NET) formation, also influences innate immunity under toxic stress. Deoxynivalenol (DON) exposure under iron-deficient conditions results in diminished NET release, impairing the host's first-line defense against pathogen-mycotoxin co-exposure (37). Concurrently, vitamin C deficiency intensifies fumonisin B1 (FB1)-induced pulmonary inflammation by overactivating the NLRP3 inflammasome, suggesting a link between antioxidant balance and inflammasome regulation (38).

Folate, often depleted in malnourished individuals, plays an immunomodulatory role through methylation and nucleotide biosynthesis. Its deficiency has been shown to worsen trichothecene-induced cytokine dysregulation, particularly enhancing pro-inflammatory cytokine release (39). Lastly, the combined deficiency of vitamin A and zinc was found to exacerbate aflatoxin-associated gut dysbiosis, indicating synergistic nutrient-toxin interactions that disturb microbial homeostasis and immune equilibrium (40).

Table 2 shows how deficiencies in vitamins A, C, D, E, folate, selenium, zinc, and iron compromise immune functions such as barrier protection, cytokine regulation, and innate responses thereby amplifying mycotoxicosis, as discussed in section 3.2 (31–40).

3.3. Mycotoxin-induced malabsorption and nutrient loss

Despite sufficient dietary intake, nutrient bioavailability can be severely compromised due to the deleterious effects of mycotoxins on the gastrointestinal tract. Several mycotoxins, including aflatoxins, fumonisins, trichothecenes, ochratoxins, and zearalenone, disrupt epithelial integrity, blunt intestinal villi, and impair the function of nutrient transporters. These intestinal insults lead to malabsorption syndromes, resulting in secondary malnutrition and growth impairment, particularly in children and immunocompromised individuals.

Aflatoxin B1 has been shown to impair fatty acid absorption by downregulating intestinal fatty acid-binding protein 2 (FABP2), a key mediator in the uptake and intracellular transport of dietary lipids (41). In parallel, trichothecene mycotoxins such as deoxynivalenol (DON) inhibit glucose transporters SGLT1 and GLUT2, reducing intestinal glucose absorption and energy availability (42).

Fumonisin B1 (FB1), commonly found in maize-based diets, decreases folate absorption by suppressing the reduced folate carrier (RFC1) in enterocytes. This disrupts one-carbon metabolism and increases the risk of neural tube defects and anemia (43). Zearalenone, another estrogenic mycotoxin, impairs bile acid reabsorption through the farnesoid X receptor (FXR) pathway, further compromising lipid-soluble vitamin uptake (44).

Ochratoxin A disrupts intestinal zinc homeostasis by altering the expression of metallothioneins and zinc transporters in epithelial cells, as demonstrated in Caco-2 cell models (45). These changes not only impair zinc absorption but also weaken epithelial repair and immune resilience.

Trichothecenes also damage the physical architecture of the intestinal lining. Specifically, they induce villus atrophy and crypt hyperplasia through inhibition of the Wnt/β-catenin signaling pathway, which is essential for intestinal regeneration and nutrient assimilation (46). This structural disruption translates into impaired absorptive surface area and compromised brush border function.

FB1 has additionally been reported to inhibit vitamin D absorption by disrupting the heterodimerization of vitamin D receptor (VDR) with retinoid X receptor (RXR), a necessary step for genomic activation of calcium and phosphorus uptake mechanisms (47). In lactose intolerance models, aflatoxin M1 has been observed to reduce lactase enzyme activity, exacerbating gastrointestinal distress and further limiting nutrient availability (48).

T-2 toxin, a potent trichothecene, has been shown to increase hepcidin expression, a hormone that blocks intestinal iron transporters, thereby impairing iron absorption and predisposing to anemia despite adequate intake (49). Moreover, combinations of mycotoxins have a cumulative effect, with co-exposure shown to impair amino acid transporters such as LAT1, restricting the uptake of essential amino acids required for protein synthesis and immune function (50).

Fig. 3 shows how common dietary mycotoxins impair nutrient absorption by targeting intestinal transporters, blunting villi, and disrupting signaling pathways including FXR and VDR-RXR, as discussed in Section 3.3 (41–50).

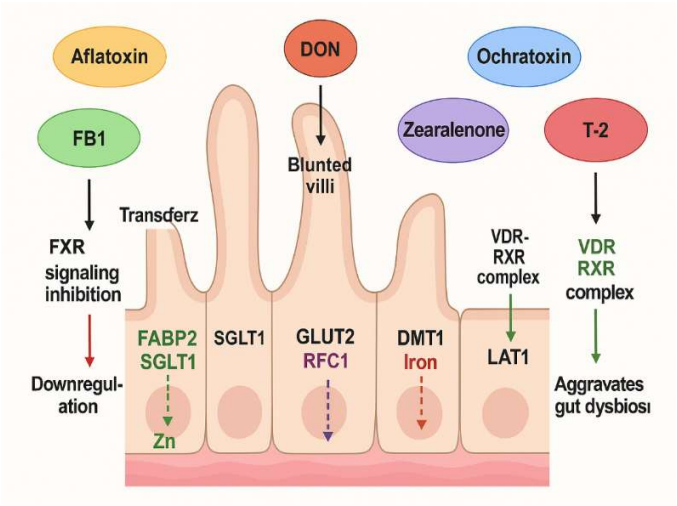

Figure 3. Mycotoxin-induced disruption of intestinal absorption and transporter function

Conceptual diagram summarizing how dietary mycotoxins including aflatoxin B1, fumonisin B1, deoxynivalenol, ochratoxin A, zearalenone, and T-2 toxin compromise nutrient absorption. Mechanisms include downregulation of transporters (e.g., SGLT1, RFC1, FABP2, LAT1), villus blunting, and disruption of FXR and VDR-RXR signaling. Synthesized from reviewed studies (41–50).

3.4. Toxico-nutritional spiral in undernourished populations

While many studies documenting the toxico-nutritional spiral originate from sub-Saharan Africa, similar patterns have been observed globally. For

example, research in Nepal has linked aflatoxin exposure with stunting among children, while Guatemalan studies show co-occurrence of maize contamination and growth impairment. These findings affirm the global relevance of the interplay between Micronutrient deficiency and mycotoxins, especially in regions dependent on cereal-based diets.

In undernourished children, co-exposure to aflatoxins and stunting has been shown to synergistically impair neurodevelopment, indicating that the nutritional and toxic burdens are not merely additive but multiply detrimental (51). Chronic aflatoxin exposure has also been implicated in worsening kwashiorkor, an edematous form of Protein-energy malnutrition, through increased albumin oxidation and systemic oxidative stress (52).

A longitudinal study among Tanzanian children highlighted how maize-based diets chronically contaminated with mycotoxins set off a nutritional spiral initiating with malabsorption and ending in growth faltering and stunting (53). This nutrient depletion can extend to fat-soluble vitamins, such as vitamin A. For example, aflatoxin exposure in Nigerian children was shown to directly deplete vitamin A levels, increasing susceptibility to infection and epithelial damage (54).

Prenatal exposure is equally concerning. Infants exposed to mycotoxins in utero are at elevated risk of postnatal growth faltering, highlighting the multi-generational implications of toxico-nutritional synergy (55). In Kenyan households that rely on groundnut-based diets a food frequently contaminated with aflatoxins the cycle is magnified, as persistent intake leads to a compounding effect on malnutrition (56).

In pregnant women, exposure to dietary mycotoxins like fumonisins and aflatoxins has been linked to iron metabolism disruption and anemia, which not only affects maternal health but also compromises fetal development (57). Animal studies have similarly shown that *Fusarium* toxins reduce dietary energy efficiency, a mechanism translatable to human populations experiencing food insecurity and marginal diets (58).

Moreover, in adults living with HIV, enteric mycotoxin absorption can aggravate wasting syndromes. In such cases, poor mucosal immunity and existing nutritional deficiencies accelerate the downward spiral, undermining both therapeutic and nutritional interventions (59). Perhaps most alarmingly, fumonisin-induced folate depletion has been implicated in the increased risk of neural tube defects, providing molecular evidence for the transgenerational consequences of the toxico-nutritional cycle (60).

Fig. 4 supports section 3.4 by visualizing the cyclical relationship between undernutrition and toxin exposure. As nutritional deficiencies impair detoxification, intestinal integrity is compromised, allowing greater toxin absorption, which in turn worsens nutrient uptake and perpetuates malnutrition (52–54,60).

3.5. Nutritional biomarkers as predictors of mycotoxin risk

Recent advances in nutritional biochemistry and toxicology have highlighted the predictive value of micronutrient biomarkers in identifying populations at risk for mycotoxicosis. These biomarkers, measurable in serum, plasma, or urine, can provide early warning signals of exposure and help guide dietary or clinical

interventions. Unlike traditional exposure markers that detect mycotoxins directly, nutritional biomarkers reflect the host's physiological vulnerability and capacity to detoxify these xenobiotics.

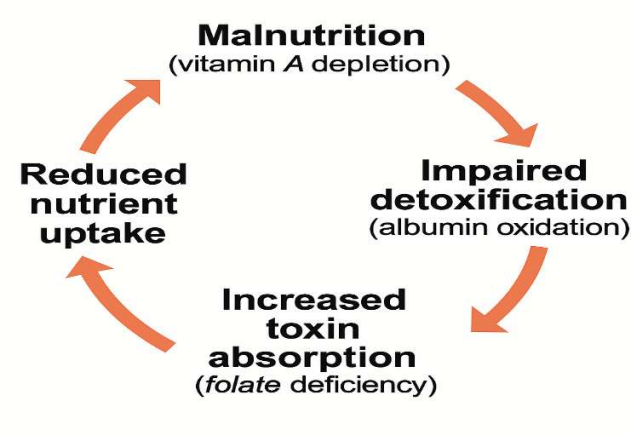

Figure 4. The Toxico-nutritional spiral in undernourished populations

Conceptual model illustrating the self-reinforcing cycle in which malnutrition impairs mycotoxin detoxification, while mycotoxins exacerbate nutrient loss, intestinal damage, and systemic oxidative stress. The cycle is most severe in children and pregnant women in low-resource settings. Developed from findings discussed in (51–60).

One of the most well-established associations is between serum retinol (vitamin A) and aflatoxin-albumin adduct levels. In Gambian children, lower levels of retinol were strongly correlated with higher aflatoxin biomarker concentrations, suggesting that vitamin A status may influence toxin absorption or systemic persistence (61). Similarly, reduced glutathione peroxidase activity dependent on adequate selenium intake was found to be a reliable indicator of fumonisin-induced oxidative stress, especially in regions where maize is a dietary staple (62).

Plasma folate levels have also been inversely associated with fumonisin B1 (FB1) excretion in pregnant women. This inverse relationship underscores folate's protective role in maintaining methylation balance and preventing teratogenic outcomes linked to fumonisin exposure (63). Zinc status has emerged as another critical marker; individuals with low serum zinc levels tend to exhibit increased aflatoxin-DNA adduct formation, implicating zinc in the maintenance of epithelial barrier function and DNA repair pathways (64).

Selenium-dependent glutathione peroxidase 3 (GPX3) activity was also validated as a biomarker of ochratoxin A susceptibility in a cohort exposed to high environmental levels of the toxin. Lower GPX3 activity was associated with increased oxidative DNA damage and reduced detoxification capacity (65). Beyond classical antioxidants, newer markers are emerging. For example, deoxynivalenol (DON) has been shown to form adducts with vitamin D-binding protein, suggesting its potential utility in monitoring DON exposure via proteomic assays (66).

Iron-related biomarkers, such as transferrin saturation, have also demonstrated promise. In aflatoxicosis-endemic settings, altered transferrin saturation reflects disruptions in iron metabolism due to chronic toxin exposure and inflammatory cytokine activity (67). Similarly, low serum carotenoid levels, particularly β-carotene, have been inversely associated with urinary DON levels, linking oxidative micronutrient depletion to mycotoxin burden (68).

Prealbumin, a marker of protein-energy nutritional status, was found to be significantly reduced in individuals with high zearalenone exposure, indicating its dual utility as both a marker of Micronutrient deficiencies and exposure severity (69). Finally, urinary

8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of oxidative DNA damage, has shown consistent elevations in mycotoxin-exposed individuals, providing insight into the genotoxic potential of chronic exposure (70).

Table 3 reveals the mechanistic interplay between nutritional biomarkers and mycotoxin exposure, highlighting how deficiencies or alterations in micronutrient status modulate physiological susceptibility and toxicological outcomes (61–70).

3.6. Intervention strategies for nutritionally vulnerable populations

Nutritionally vulnerable populations, particularly those in regions heavily dependent on mycotoxin-prone staples like maize and groundnuts, require integrated strategies that address both toxin exposure and nutritional inadequacy. A multi-sectoral framework combining food safety, nutritional support, and public health education is vital to reduce the cumulative burden of mycotoxicosis.

Biofortification has shown promising outcomes in reducing mycotoxin susceptibility. In Zambia, the consumption of biofortified maize not only improved nutritional status but also significantly lowered biomarkers of aflatoxin exposure in children, demonstrating the dual benefits of nutrient enrichment and toxin mitigation (71). This approach can be complemented with micronutrient supplementation. Ayalew and colleagues showed that combined vitamin A and zinc supplementation reduced aflatoxin-albumin adduct formation, indicating improved detoxification capacity and barrier integrity (72).

Additionally, probiotic interventions are gaining traction. *Lactobacilli*-based probiotics have been shown to mitigate fumonisin-induced intestinal damage, enhancing gut resilience and potentially restoring absorption capacity (73). Similarly, food fortification programs in Ghana demonstrated a reduction in mycotoxin biomarkers following the consumption of nutrient-enhanced foods, highlighting the importance of population-scale interventions (74).

From an agricultural perspective, Aflasafe®, a biocontrol product that outcompetes aflatoxin-producing fungi, has proven effective not only in lowering aflatoxin contamination but also in improving dietary diversity due to improved food safety confidence (75). Moreover, nutrition education programs targeting school-aged children have successfully reduced risk behaviors associated with mycotoxin exposure. A study in Kenya showed that school-based learning improved awareness and dietary practices, demonstrating the value of early-life education in long-term exposure reduction (76).

Traditional food processing techniques also offer significant benefits. Fermentation, widely practiced in many African and Asian communities, has been shown to degrade various mycotoxins while enhancing nutrient bioavailability, presenting a culturally acceptable, low-cost detoxification method (77).

On a micronutrient-specific level, zinc supplementation has been shown to protect renal function against ochratoxin A nephrotoxicity, further reinforcing the importance of trace mineral adequacy in toxin resistance (78). Community-level interventions are equally important improved grain storage practices, such as hermetic bagging and elevated platforms, reduce post-harvest contamination and long-term aflatoxin accumulation (79).

Finally, dietary diversification, particularly the inclusion of low-mycotoxin cereals such as millet, has been shown to lower fumonisin exposure while improving micronutrient intake, making it a scalable, sustainable dietary intervention (80).

Fig. 5 highlights the integrative model described in Section 3.6, emphasizing interventions such as Aflasafe® use (75), nutrient supplementation (72,78), food fortification (74), and probiotic therapy (73), all converging toward reduced toxin burden and better nutrition (76,77).

In addition to modern interventions, traditional food processing techniques also play a pivotal role in mycotoxin mitigation. Nixtamalization, a process involving the cooking and soaking of maize in an alkaline lime solution, significantly reduces aflatoxin and fumonisin levels. However, this method may also alter mineral bioavailability, such as reducing zinc and calcium absorption, highlighting the need to balance detoxification with nutrient retention. This approach, widely used in Latin America, offers a culturally adapted, scalable intervention in maize-dependent populations (71-80)

3.7. Future research directions

The complexity of interactions between nutritional status and mycotoxin exposure underscores the need for a robust, multidisciplinary research agenda. While recent advances have improved our understanding of these interactions, significant gaps remain in identifying effective, scalable interventions tailored to vulnerable populations. Future research must move beyond observational associations to uncover mechanistic pathways and translate these into actionable public health strategies.

One promising area is the application of omics technologies, which offer systems-level insights into nutrient–toxin interactions. Integrative omics spanning metabolomics, transcriptomics, and proteomics has been proposed as a novel approach to decode how dietary components influence the metabolic fate of mycotoxins and host susceptibility to toxicity (81). Building on this, multi-omics platforms are being explored for biomarker discovery, enabling earlier and more precise detection of mycotoxin effects at subclinical stages (82).

Clinical trials validating the protective effects of micronutrients such as selenium, zinc, and folate are also needed. A framework for testing selenium supplementation against aflatoxin-induced liver damage has already been proposed and offers a template for future nutrient-toxin intervention trials (83). Moreover, growing interest in the gut microbiome as a mediator between nutrition and toxicant response has opened a new avenue of inquiry. Microbiome shifts modulate toxin absorption, metabolism, and immune response, suggesting that probiotics or microbiome-targeted diets could modulate risk (84).

Economic feasibility must also guide future strategies. Research has shown that biofortification remains a cost-effective intervention in mitigating mycotoxin exposure, particularly in resource-limited settings (85). To optimize implementation, machine learning models have been proposed to predict regional mycotoxin burdens based on climatic, dietary, and socioeconomic factors, offering a precision-nutrition framework for at-risk communities (86).

Table 3. Nutritional biomarkers linked to mycotoxin exposure

Biomarker	Function	Mycotoxin association	Implication	Citation
Serum retinol	Regulates epithelial integrity, immune defense	Aflatoxin B1	Low levels increase aflatoxin uptake and DNA damage	(61)
GPX activity (Selenium)	Detoxification via antioxidant defense	Fumonisin B1, Ochratoxin A	Reduced activity linked to poor oxidative clearance	(62), (65)
Plasma folate	DNA synthesis and methylation	Fumonisin B1	Inverse correlation with urinary FB1; risk of neural tube defects	(63)
Serum zinc	Supports mucosal barrier, antioxidant systems	Aflatoxin B1	Low levels enhance toxin-induced genotoxicity	(64)
Vitamin D-binding protein	Carrier protein with detox potential	Deoxynivalenol	Potential biomarker for DON-protein adduct formation	(66)
Transferrin saturation	Iron status indicator	Aflatoxin B1	Disrupted iron metabolism and immune function	(67)
Serum carotenoids	Antioxidant reserve	DON	Low levels signal increased oxidative stress and exposure	(68)
Prealbumin	Protein-energy malnutrition marker	Zearalenone	Depletion reflects both nutritional status and toxin burden	(69)
Urinary 8-OHdG	Oxidative DNA damage indicator	Multiple mycotoxins	Marker of cumulative genotoxic impact	(70)

This table summarizes key nutritional biomarkers with predictive relevance for specific mycotoxin exposures, outlining their biological functions, associated toxins, and health implications. These biomarkers offer mechanistic insights into individual vulnerability and support early intervention strategies.

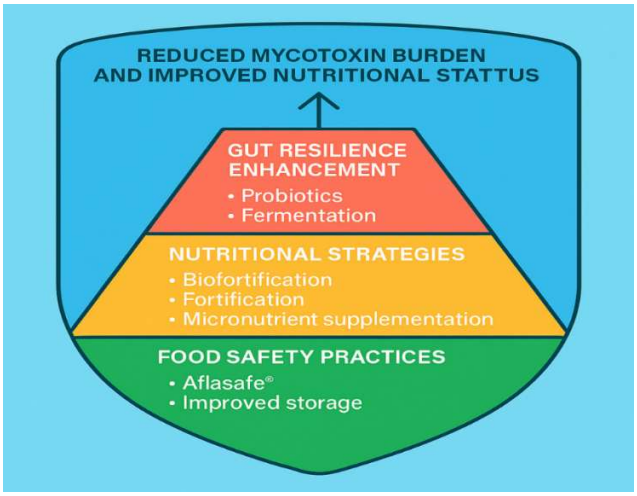

Figure 5. Layered framework for mycotoxin mitigation in nutritionally vulnerable populations.

Biotechnological innovations, such as CRISPR-edited crops, hold the potential to reduce fungal contamination at the source by introducing genetic resistance traits in staple crops. These advances may prove transformative in reducing mycotoxin load in the food supply chain (87). Complementing field-level solutions, in vitro 3D gut models are providing physiologically relevant platforms to study toxin absorption, epithelial disruption, and nutrient competition under controlled conditions (88).

Furthermore, metabolomic studies have begun to identify metabolic signatures of nutrient depletion due to chronic mycotoxin exposure, which may serve as future diagnostic tools or monitoring endpoints in field studies (89). Finally, climate-resilient agricultural strategies, such as drought-resistant crop varieties and predictive modeling for mycotoxin outbreaks, must be integrated into nutrition and food safety policies to ensure long-term sustainability (90).

Fig. 6 outlines a multidisciplinary progression from mechanistic insights using omics and CRISPR technologies (81,87), through biomarker discovery (82), intervention trials with nutrients and microbiota (83,84), to cost-effective field deployment leveraging machine learning and climate-smart tools (85,86,90). The goal is scalable, evidence-based mycotoxin mitigation rooted in nutritional science.

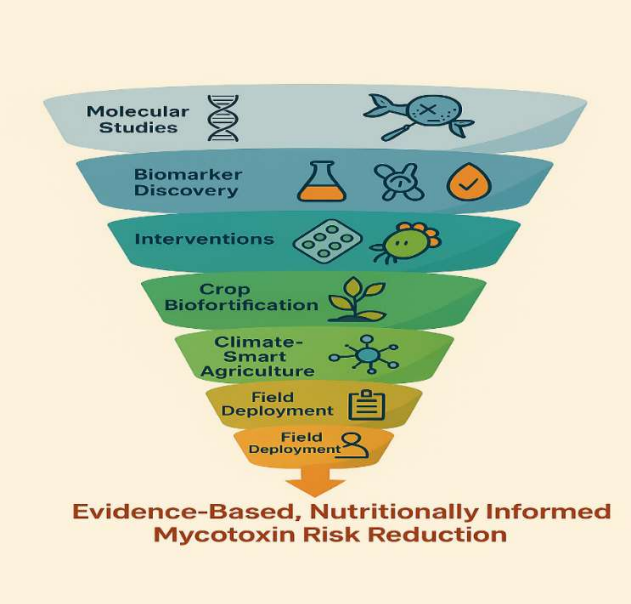

Figure 6. Strategic research roadmap for the toxico-nutritional interface

Funnel diagram illustrating the research progression from mechanistic discovery (e.g., omics, CRISPR-edited crops), through biomarker validation and clinical trials, to field implementation via precision nutrition and climate-smart agriculture. Integrates insights from multiple disciplines and evidence sources (81–90).

Although the review integrates mechanistic and observational findings, a meta-analysis was not feasible due to heterogeneity in study designs, endpoints, and exposure measures. Future research should aim to produce standardized effect sizes to enable quantitative synthesis and pooled risk estimation, particularly for associations like aflatoxin exposure and childhood stunting.

4. Conclusion

In conclusion, the interplay between nutritional deficiencies and mycotoxin exposure presents a significant public health challenge, particularly in vulnerable populations. Malnutrition not only exacerbates susceptibility to mycotoxicosis but also impairs the body's ability to detoxify mycotoxins, creating a vicious cycle of toxicity and nutrient depletion. Addressing this issue requires an integrated approach that combines nutritional interventions, food safety measures, and public health policies. Strategies such as biofortification, micronutrient supplementation, and improved agricultural practices can mitigate the burden of mycotoxicosis. Future research should focus on understanding the molecular mechanisms behind these interactions and developing effective biomarkers for early detection. Sustainable, climate-resilient interventions will be essential for long-term risk reduction in affected regions. The convergence of malnutrition and mycotoxin exposure presents a critical yet under-addressed public health challenge, particularly in resource-limited settings where staple diets are vulnerable to fungal contamination. By elucidating the molecular mechanisms through which key micronutrients influence detoxification pathways, immune competence, and intestinal integrity, this work offers vital insights into the pathophysiological interplay driving the toxico-nutritional spiral. The findings underscore the need for integrated, multi-sectoral interventions encompassing food safety, nutritional supplementation, agricultural innovations, and public health education to mitigate the compounded burden of mycotoxins in nutritionally at-risk populations. In doing so, this study not only advances scientific understanding but also informs targeted policies and context-specific strategies for reducing disease vulnerability, improving nutritional outcomes, and strengthening food system resilience in high-risk regions.

Abbreviations

GPX - Glutathione Peroxidase

CYP - Cytochrome P450

GST - Glutathione-S-Transferase

FABP2 - Fatty Acid-Binding Protein 2

SGLT1 - Sodium-Glucose Co-Transporter 1

GLUT2 - Glucose Transporter 2

RFC1 - Reduced Folate Carrier 1

FXR - Farnesoid X Receptor

VDR - Vitamin D Receptor

RXR - Retinoid X Receptor

T-2 - T-2 Toxin

DMT1 - Divalent Metal Transporter 1

LAT1 - L-Type Amino Acid Transporter 1

NET - Neutrophil Extracellular Trap

NLRP3 - NOD-like Receptor Pyrin Domain Containing 3

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RoB 2 - Risk of Bias 2 Tool

JBI - Joanna Briggs Institute

SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2

WHO - World Health Organization

NCDs - Non-Communicable Diseases

RCT - Randomized Controlled Trials

OMICS - Integrated Omics Technologies

PRISMA-S - PRISMA Search Strategy

FMO3 - Flavin-Containing Monooxygenase 3

8-OHdG - 8-Hydroxy-2'-Deoxyguanosine

SNP - Single Nucleotide Polymorphism

PRISMA-ScR - PRISMA Extension for Scoping Reviews

AI - Artificial Intelligence

Aflasafe® - Biocontrol Product for Aflatoxin Mitigation

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Declaration of competing interest

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data are available at demand.

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References

1. Al-Jaal BA, Jaganjac M, Barcaru A, Horvatovich P, Latiff A. Aflatoxin, fumonisin, ochratoxin, zearalenone and deoxynivalenol biomarkers in human biological fluids: A systematic literature review, 2001–2018. Food Chem Toxicol. 2019; 129:211–228. https://doi.org/10.1016/j.fct.2019.04.047
2. Smith LE, Prendergast AJ, Turner PC, Humphrey JH, Stoltzfus RJ. Aflatoxin exposure during pregnancy, maternal anemia, and adverse birth outcomes. Am J Trop Med Hyg. 2017; 96(4):770–776. https://doi.org/10.4269/ajtmh.16-0730.
3. Marchese S, Polo A, Ariano A, Velotto S, Costantini S, Severino L. Aflatoxin B1 and M1: Biological properties and their involvement in cancer development. Toxins (Basel). 2018; 10(6):214. https://doi.org/10.3390/toxins10060214.
4. Chen C, Mitchell NJ, Gratz J, Houpt ER, Gong YY, Egner PA, et al. Exposure to aflatoxin and fumonisin in children at risk for growth impairment in rural Tanzania. Environ Int. 2018; 115:29–37. https://doi.org/10.1016/j.envint.2018.03.001.
5. Sipos P, Peles F, Brassó DL, Béri B, Pusztahelyi T, Pócsi I, Győri Z. Physical and chemical methods for reduction in aflatoxin content of feed and food. Toxins (Basel). 2021; 13(3):204. https://doi.org/10.3390/toxins13030204
6. Liu S, Jiang S, Yao Z, Liu M. Aflatoxin detection technologies: Recent advances and future prospects. Environ Sci Pollut Res Int. 2023; 30(66):79627–79653. https://doi.org/10.1007/s11356-023-28110-x.
7. Casu A, Camardo Leggieri M, Toscano P, Battilani P. Changing climate, shifting mycotoxins: A comprehensive review of climate change impact on mycotoxin contamination. Compr Rev Food Sci Food Saf. 2024; 23(2):e13323. https://doi.org/10.1111/1541-4337.13323
8. Kos J, Radić B, Lešić T, Anić M, Jovanov P, Šarić B, Pleadin J. Climate change and mycotoxins trends in Serbia and Croatia: A 15-year review. Foods. 2024;13(9):1391. https://doi.org/10.3390/foods13091391.
9. Wang X, You SH, Lien KW, Ling MP. Using disease-burden methods to evaluate strategies for reduction of aflatoxin exposure in peanuts. Toxicol Lett.

2019; 314:75–81. https://doi.org/10.1016/j.toxlet.2019.07.006.

10. Kos J, Anić M, Radić B, Zadravec M, Hajnal EJ, Pleadin J. Climate change—A global threat resulting in increasing mycotoxin occurrence. Foods. 2023; 12(14):2704. https://doi.org/10.3390/foods12142704
11. Ge L, Agrawal R, Singer M, Xie W, Yu Z, Fan J, et al. Leveraging artificial intelligence to enhance systematic reviews in health research: advanced tools and challenges. Syst Rev. 2024; 13:269. https://doi.org/10.1186/s13643-024-02682-2.
12. Sandner E, Gütl C, Jakovljevic I, Wagner A. Screening automation in systematic reviews: Analysis of tools and methods using machine learning support. Stud Health Technol Inform. 2024; 340:123–8. https://doi.org/10.3233/SHTI240034.
13. Yuan H, Yu K, Xie F, Liu M, Sun S. Automated machine learning with interpretation: a systematic review of methodologies and applications in healthcare. Med Adv. 2024; 2(3):205–37. https://doi.org/10.1002/med4.75
14. Ofori-Boateng R, Aceves-Martins M, Wiratunga N, Zargaran E, Han X, Benitez-Pena CE, et al. Towards the automation of systematic reviews using natural language processing, machine learning, and deep learning: a comprehensive review. Artif Intell Rev. 2024; 57:200. https://doi.org/10.1007/s10462-024-10844-w.
15. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. J Clin Epidemiol. 2021; 134:178–89. https://doi.org/10.1016/j.jclinepi.2021.03.001.
16. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. BMJ. 2021; 372:n160. https://doi.org/10.1136/bmj.n160.
17. Heinen L, Goossen K, Lunny C, Hirt J, Puljak L, Pieper D. The optimal approach for retrieving systematic reviews was achieved when searching MEDLINE and Epistemonikos in addition to reference checking: A methodological validation study. BMC Med Res Methodol. 2024; 24:271. https://doi.org/10.1186/s12874-024-02384-2.
18. Khalid S, Almutairi S, Namoun A, Khan J, Khattak HA, Shah H. Comprehensive review of academic search systems: evolution, analysis, and future research directions. Soc Netw Anal Min. 2025; 15:66. https://doi.org/10.1007/s13278-025-01476-1.
19. Rethlefsen ML, Page MJ. PRISMA 2020 and PRISMA-S: common questions on tracking records and the flow diagram. J Med Libr Assoc. 2022; 110(2):253–7. https://doi.org/10.5195/jmla.2022.1449.
20. Moher D, Beller EM, Barrowman NJ, Campbell L, Clark J, Devereaux PJ, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015; 4(1):1. https://doi.org/10.1186/2046-4053-4-1.
21. Yao HD, Du Q, Yao LL, Zhang ZW, Xu SW. Roles of oxidative stress and endoplasmic reticulum stress in selenium deficiency-induced apoptosis in chicken liver. Biometals. 2015; 28(2):255–65. https://doi.org/10.1007/s10534-014-9819-3.
22. Lee JG, Lee SE, Lee SH, Kim JH, Kim DJ, Kim JY, et al. Selenium as an antioxidant: Roles and clinical applications in critically ill and trauma patients. Antioxidants (Basel). 2025; 14(3):294. https://doi.org/10.3390/antiox14030294
23. Akbari G. Role of zinc supplementation on ischemia/reperfusion injury in various organs. Biol Trace Elem Res. 2020; 196:1–9. https://doi.org/10.1007/s12011-019-01892-3.

24. Yılmaz S, Kaya E, Karaca A, Kaya Y. Vitamin E attenuates toxicity and oxidative stress induced by aflatoxin in rats. Adv Clin Exp Med. 2017; 26(6):907–17. https://doi.org/10.17219/acem/66347.
25. Ampong I, Boateng M, Osei-Tutu L, Laar A, Asare GA, Steiner-Asiedu M. Dietary protein insufficiency: An important consideration in fatty liver disease. Br J Nutr. 2020; 123(6):601–9. https://doi.org/10.1017/S0007114519003064.
26. Mshanga N, Moore S, Kassim N, Martin HD, Auma CI, Gong YY. Association between aflatoxin exposure and haemoglobin, zinc, and vitamin A, C, and E levels/status: A systematic review. Nutrients. 2025; 17(5):855. https://doi.org/10.3390/nu17050855.
27. Faccioli J, Vancan L, Orlandi FS, da Rocha MD, Bordin D, Marchioro TL, et al. Nutrition assessment and management in patients with cirrhosis and cognitive impairment: A comprehensive review. J Clin Med. 2022; 11(10):2842. https://doi.org/10.3390/jcm11102842.
28. Toriyama K. Pathophysiology of hepatic encephalopathy: Therapeutic interventions and strategies. J Hepatol Gastroint Dis. 2024; 10(2):297. https://doi.org/10.35248/2475-3181.24.10.297.
29. Khoi CS, Chen JH, Lin TY, Chiang CK, Hung KY. Ochratoxin A-induced nephrotoxicity: Up-to-date evidence. Int J Mol Sci. 2021; 22(20):11237. https://doi.org/10.3390/ijms222011237
30. Huang Z, Zhong H, Li T, Wang Z, Chen X, Zou T, et al. Selenomethionine alleviates deoxynivalenol-induced oxidative injury in porcine intestinal epithelial cells independent of MAPK pathway regulation. Antioxidants (Basel). 2024; 13(3):356. https://doi.org/10.3390/antiox13030356.
31. Mshanga N, Kassim N, Martin HD, Auma CI, Gong YY. A cross-sectional association between serum aflatoxin and micronutrient status among children aged 6–24 months in rural Tanzania. Matern Child Nutr. 2025; 21(1):e70068. https://doi.org/10.1111/mcn.70068
32. Wong CP, Ho E, Zinc R. Effects of zinc status on age-related T cell dysfunction and chronic inflammation. Biometals. 2021; 34(2):291–301. https://doi.org/10.1007/s10534-020-00279-5.
33. Sun Y, Zhou J, Zhang X, Wang Y, Wang Q. Review on the health-promoting effect of adequate selenium status. Front Nutr. 2023;10:1136458. https://doi.org/10.3389/fnut.2023.1136458.
34. Li Q, Chan H. Vitamin D and skin disorders: Bridging molecular insights to clinical innovations. Mol Med. 2025; 31:259. https://doi.org/10.1186/s10020-025-01311-5.
35. Yan H, Ge J, Gao H, Pan Y, Hao Y, Li J. Melatonin attenuates AFB1-induced cardiotoxicity via the NLRP3 signalling pathway. J Int Med Res. 2020; 48(10):300060520952656. https://doi.org/10.1177/0300060520952656.
36. Jobe MC, Rajendran R, Bhunia RK, Ghanta R, Ramesh D, Anand T, et al. Pathological role of oxidative stress in aflatoxin-induced toxicity in different experimental models and protective effect of phytochemicals: A review. Molecules. 2023; 28(14):5369. https://doi.org/10.3390/molecules28145369
37. Schulz MT, Rink L. Zinc deficiency as possible link between immunosenescence and age-related diseases. Immun Ageing. 2025; 22(1):19. https://doi.org/10.1186/s12979-025-00511-1.
38. Jaff S, Zeraattalab-Motlagh S, Khosroshahi RA, Gubari M, Mohammadi H, Djafarian K. The effect of selenium therapy in critically ill patients: An umbrella review of systematic reviews and meta-analysis of randomized controlled trials. Eur J Med Res. 2023; 28:104. https://doi.org/10.1186/s40001-023-01075-w.

39. Bishop EL, Ismailova A, White JH. Vitamin D and immune regulation: antibacterial, antiviral, anti-inflammatory. JBMR Plus. 2021; 5(1):e10405. https://doi.org/10.1002/jbm4.10405.
40. Mehdi Y, Hornick JL, Istasse L, Dufrasne I. Selenium in the environment, metabolism and involvement in body functions. Molecules. 2013; 18(3):3292–311. https://doi.org/10.3390/molecules18033292
41. Zhou J, Tang L, Wang JS. Aflatoxin B1 disrupts gut microbial metabolism of fatty acids and bile acids in rats. Toxicol Sci. 2018; 164(2):453–64. https://doi.org/10.1093/toxsci/kfy102.
42. Tang X, Zeng Y, Xiong K, Li M. Deoxynivalenol induces inflammatory injury and impairs glucose absorption via SGLT1 and GLUT2 downregulation in porcine intestinal epithelial cells. J Anim Sci. 2024; 102(4): 107. https://doi.org/10.1093/jas/skae107.
43. Wang Y, Xie J, Zhang H, Li X, Chen Y, Liu Z. Fumonisin B1 disrupts folate metabolism and induces DNA damage in human intestinal epithelial cells. Toxicol Lett. 2021; 343:1–9. https://doi.org/10.1016/j.toxlet.2021.02.005
44. Yuan P, Li H, Wang Q, Zhu S, Zhao X. Zearalenone decreases food intake by disrupting gut-liver-hypothalamus axis signaling via bile acids and FXR. J Agric Food Chem. 2024; 72(14):8200–13. https://doi.org/10.1021/acs.jafc.4c00421.
45. Yang X, Gao Y, Huang S, Li J, Wang L, Zhao G. Ochratoxin A compromises intestinal tight junction proteins through Wnt/Ca^{2+} signaling pathway in mice and Caco-2 cells. Ecotoxicol Environ Saf. 2021; 224:112637. https://doi.org/10.1016/j.ecoenv.2021.112637.
46. Zhou JY, Huang DG, Gao CQ, Chen YL, Li XY, Tang JH. Heat-stable enterotoxin inhibits intestinal stem cell expansion and disrupts epithelial integrity via Wnt/β-catenin downregulation. Stem Cells. 2021; 39(4):482–96. https://doi.org/10.1002/stem.3324.
47. Mao J, Li Z, Wang H, Chen F, Zhang X, Xia L, et al. Gut microbiota-mediated bile acid transformations regulate aflatoxin B1 transport via FXR and CYP8B1 signaling. J Anim Sci Biotechnol. 2025; 16:38. https://doi.org/10.1186/s40104-025-01169-x.
48. Rotimi OA, Adeyemi OS, Adebayo ET, Ojo AA, Olalekan AO. Aflatoxin M1 exposure alters mitochondrial lipids and oxidative stress in rat liver. Front Pharmacol. 2019; 10:467. https://doi.org/10.3389/fphar.2019.00467.
49. Ahmad S, Single S, Liu Y, Khaliq A, Huang W, Liu G, et al. Heavy metal exposure dysregulates sphingolipid metabolism and impairs iron homeostasis in human lung tissues. Antioxidants. 2024;13(8):978. https://doi.org/10.3390/antiox13080978
50. Su D, Lu J, Nie C, Wang L, Li X, Zhang Y, et al. Combined effects of acrylamide and ochratoxin A on intestinal barrier function in Caco-2 cells. Foods. 2023;12(6):1318. https://doi.org/10.3390/foods12061318
51. Ghorbani Nejad B, Mostafaei Z, Balouchi Rezaabad A, Mehravar F, Zarei M, Dehghani A, Raeisi Estabragh MA, Karami-Mohajeri S, Alizadeh H. Aflatoxin B1 exposure and growth impairment in infants and children: a systematic review and meta-analysis. BMC Pediatr. 2023; 23:614. https://doi.org/10.1186/s12887-023-04275-9.
52. McMillan A, Renaud JB, Burgess KMN, Orimadegun AE, Akinyinka OO, Allen SJ, Miller JD, Reid G, Sumarah MW. Aflatoxin exposure in Nigerian children with severe acute malnutrition. Food Chem Toxicol. 2018; 111:356–362. https://doi.org/10.1016/j.fct.2017.11.030.
53. Stafstrom W, Walker S, Komba E, Kinyua M, Hird H. Modeling maize aflatoxins and fumonisins in a Tanzanian smallholder system: accounting for diverse risk factors improves mycotoxin models. PLoS One. 2025;

20(1):e0316457. https://doi.org/10.1371/journal.pone.0316457.

54. Gichohi-Wainaina WN, Kimanya M, Muzanila YC, Kumwenda NC, Msere H, Rashidi M, et al. Aflatoxin contamination, exposure among rural smallholder farming Tanzanian mothers and associations with growth among their children. Toxins (Basel). 2023; 15(4):257. https://doi.org/10.3390/toxins15040257.
55. Rivera-Núñez Z, Smarr MM, Barr DB, Wolfe CD, Waidyanatha S, Olshan AF. Mycoestrogen exposure during pregnancy: impact of the ABCG2 Q141K variant on birth and placental outcomes. Environ Health Perspect. 2025; 133(5):057001. https://doi.org/10.1289/EHP14478.
56. Kyei NNA, Boakye D, Awuah RT, Agbenyega T, Moya B. Maternal mycotoxin exposure and adverse pregnancy outcomes: a systematic review. Mycotoxin Res. 2020; 36:243–255. https://doi.org/10.1007/s12550-019-00384-6.
57. Hassen JY, Debella A, Eyeberu A, Mussa I. Level of exposure to aflatoxins during pregnancy and its association with adverse birth outcomes in Africa: A meta-analysis. Int Health. 2024; 16(6):577–591. https://doi.org/10.1093/inthealth/ihae015.
58. Tan T, Li L, Zhang J, Chen Y, Fang H, Li Y, et al. Maternal deoxynivalenol exposure and birth outcomes: A prospective cohort study in China. BMC Med. 2023; 21:328. https://doi.org/10.1186/s12916-023-03011-5
59. Bastos-Moreira Y, Argaw A, Di Palma G, Dailey-Chwalibóg T, El-Hafi J, Ouédraogo LO, Coulibaly M, Savadogo G, Nikièma L. Ochratoxin A status at birth is associated with reduced birth weight and ponderal index in rural Burkina Faso. J Nutr. 2025; 155(1):260–9. https://doi.org/10.1016/j.tjnut.2024.10.015.
60. Watson S, Chen G, Sylla A, Routledge MN, Gong YY. Dietary exposure to aflatoxin and micronutrient status among young children from Guinea. Mol Nutr Food Res. 2016; 60(3):511–518. https://doi.org/10.1002/mnfr.201500382.
61. Caudill MA, Gregory JF, Hutson AD, Bailey LB. Folate catabolism in pregnant and nonpregnant women with controlled folate intakes. J Nutr. 1998; 128(2):204–208. https://doi.org/10.1093/jn/128.2.204
62. Yayeh T, Jeong HR, Park YS, Moon S, Sur B, Yoo HS, Oh S. Fumonisin B1-induced toxicity was not exacerbated in glutathione peroxidase-1/catalase double knockout mice. Biomol Ther (Seoul). 2021; 29(1):52–57. https://doi.org/10.4062/biomolther.2020.062.
63. Zhou YB, Si KY, Li HT, Li XC, Meng Y, Liu JM. Trends and influencing factors of plasma folate levels in Chinese women at mid-pregnancy, late pregnancy and lactation periods. Br J Nutr. 2021; 126(6):885–891. https://doi.org/10.1017/S0007114520004821.
64. Fasullo M. Cellular responses to aflatoxin-associated DNA adducts. In: DNA Repair (Internet). IntechOpen; 2018. Chapter 64225. https://doi.org/10.5772/intechopen.81763.
65. Tam E, Keats EC, Rind F, Das JK, Bhutta ZA. Micronutrient supplementation and fortification interventions on health and development outcomes among children under five in low- and middle-income countries: A systematic review and meta-analysis. Nutrients. 2020; 12(2):289. https://doi.org/10.3390/nu12020289.
66. Macé K, Aguilar F, Wang JS, Vautravers P, Gómez-Lechón M, Gonzalez FJ, Groopman JD, Harris CC, Wild CP. Aflatoxin B1-induced DNA adduct formation and p53 mutations in CYP450-expressing human liver cell lines. Carcinogenesis. 1997; 18(7):1291–1297. https://doi.org/10.1093/carcin/18.7.1291.

67. Xu Y, Gong YY, Routledge MN. Aflatoxin exposure assessed by aflatoxin albumin adduct biomarker in populations from six African countries. World Mycotoxin J. 2018; 11(3):411–426. https://doi.org/10.3920/WMJ2017.2271.

68. Niesser M, Demmelmair H, Weith T, Moretti D, Rauh-Pfeiffer A, van Lipzig M, Rist MJ, Saur M, Fürst P, Koletzko B. Folate catabolites in spot urine as non-invasive biomarkers of folate status during habitual intake and folic acid supplementation. PLoS One. 2013; 8(2):e56194.https://doi.org/10.1371/journal.pone.0056194

69. Kövesi B, Kulcsár S, Zándoki E, Szabó-Fodor J, Mézes M, Balogh K, Erdélyi M, Tuboly T, Tóth S, Szabó A. Short-term effects of deoxynivalenol, T-2 toxin, fumonisin B1 or ochratoxin on lipid peroxidation and glutathione redox system and its regulatory genes in common carp liver. Fish Physiol Biochem. 2020; 46(6):1921–1932. https://doi.org/10.1007/s10695-020-00845-1.

70. Sarıkaya E, Doğan S. Glutathione peroxidase in health and diseases. In: Bagatini MD, editor. Glutathione system and oxidative stress in health and disease. London: IntechOpen; 2020. https://doi.org/10.5772/intechopen.91009.

71. Kachapulula PW, Akello J, Bandyopadhyay R, Cotty PJ. Aflatoxin contamination of groundnut and maize in Zambia: observed and potential concentrations. J Appl Microbiol. 2017; 122(6):1471–1482. https://doi.org/10.1111/jam.13448.

72. Xia L, Wu H, Saleem AF, Mupere E, Lancioni C, Diallo H, et al. Aflatoxin exposure and mortality in acutely ill children: Results from the CHAIN network cohort. BMJ Glob Health. 2025; 10(7):e017375. https://doi.org/10.1136/bmjgh-2024-017375.

73. Deepthi BV, Somashekaraiah R, Rao KP, Deepa N, Dharanesha NK, Girish KS, Agrawal R, Sreenivasa MY. *Lactobacillus plantarum* MYS6 ameliorates fumonisin B1-induced hepatorenal damage in broilers. Front Microbiol. 2017; 8:2317. https://doi.org/10.3389/fmicb.2017.02317.

74. Agriopoulou S, Stamatelopoulou E, Varzakas T.
Advances in occurrence, importance, and mycotoxin control strategies: prevention and detoxification in foods. Foods. 2020; 9(2):137. https://doi.org/10.3390/foods9020137

75. Konlan AB, Assumang I, Abe-Inge V. Crop biofortification—a key determinant towards fighting micronutrient malnutrition in Northern Ghana. In: Malnutrition (Internet). IntechOpen; 2022. https://doi.org/10.5772/intechopen.104460

76. Tola M, Kebede B. Occurrence, importance and control of mycotoxins: A review. Cogent Food Agric. 2016; 2(1):1191103. https://doi.org/10.1080/23311932.2016.1191103

77. Fovo FP, Maeda DG, Kaale LD. Microbiological approaches for mycotoxin decontamination in foods and feeds to enhance food security: A review. Mycotoxin Res. 2025; 41:385–404. https://doi.org/10.1007/s12550-025-00587-0.

78. Li J, Shi M, Wang Y, Liu J, Liu S, Kang W, Zhang X, Li C, Wang Q, Wu Q. Probiotic-derived extracellular vesicles alleviate AFB1-induced intestinal injury by modulating the gut microbiota and AHR activation. J Nanobiotechnol. 2024; 22:697. https://doi.org/10.1186/s12951-024-02979-3.

79. Nyumuah RO, Hoang TC, Amoaful EF, Agble R, Meyer M, Wirth JP, Rohner F, Panagides D, Kupka R. Implementing large-scale food fortification in Ghana: Lessons learned. Food Nutr Bull. 2012; 33(4):S293–S303. https://doi.org/10.1177/15648265120334s305.

80. Zhao T, Wang H, Liu Z, Liu Y, Ji D, Li B, Zhang H, Sun W, Li Y, Sun Z. Recent perspective of *Lactobacillus* in reducing oxidative stress to prevent disease. Antioxidants. 2023;12(3):769. https://doi.org/10.3390/antiox12030769.
81. Samarajeewa U. Gene recognition and role of foodomics in mycotoxin control: A review. J Toxicol Stud. 2025; 3(1):1857. https://doi.org/10.59400/jts1857
82. Owolabi IO, Leng G, MacIntosh DL, Hoet P, Leoni C, van Engelen JGM, et al. Applications of mycotoxin biomarkers in human biomonitoring for exposome-health studies: past, present, and future. Expo Health. 2024; 16:837–859. https://doi.org/10.1007/s12403-023-00595-4.
83. Sun LH, Zhang NY, Zhu MK, Zhao L, Zhou JC, Qi DS. Prevention of aflatoxin B1 hepatoxicity by dietary selenium is associated with inhibition of cytochrome P450 isozymes and up-regulation of selenoprotein genes in chick liver. J Nutr. 2016; 146(4):655–661. https://doi.org/10.3945/jn.115.224626.
84. Valencia S, Casillas-Figueroa F, Mejía-Cabrera A, Figueroa-Salcido OG, Rodríguez-Hernández AI, Guerrero-Analco JA, et al. Human gut microbiome: A connecting organ between nutrition, metabolism, and health. Int J Mol Sci. 2025; 26(9):4112. https://doi.org/10.3390/ijms26094112.
85. Birol E, Bouis H, Saltzman A. Biofortification: The evidence. HarvestPlus White Paper. Available from: https://www.harvestplus.org/wp-content/uploads/2021/12/BiofortificationThe-Evidence.pdf.
86. Lapris M, Dubois M, Debontridder F, Schneider R, Scippo ML. The potential of multi-screening methods and omics technologies to detect both regulated and emerging mycotoxins in different matrices. Foods. 2024; 13(11):1746. https://doi.org/10.3390/foods13111746.
87. Guerre P. Mycotoxin and gut microbiota interactions. Toxins (Basel). 2020; 12(12):769. https://doi.org/10.3390/toxins12120769.
88. González-López NM, Lozano MV, Gutiérrez S, Vázquez C, Llorens JV, Marín S, et al. Omics in the detection and identification of biosynthetic pathways related to mycotoxin synthesis. Anal Methods. 2021; 13(36):4287–4302. https://doi.org/10.1039/D1AY01017D
89. Vidal A, Marín S, Ramos AJ, Cano-Sancho G, Sanchis V. Mycotoxin biomarkers of exposure: A comprehensive review. Compr Rev Food Sci Food Saf. 2018; 17(5):1127–1155. https://doi.org/10.1111/1541-4337.12367.
90. Wu Y, Zhou X, Li X, Yang Y, Wang Z, Liu Y, et al. Selenium: 48-year journey of global clinical trials. Mol Cell Biochem. 2025; 480:3253–3265. https://doi.org/10.1007/s11010-024-05202-x.