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Biochemical interplay between gut microbiota, nutritional modulators, and mycotoxin detoxification, a triadic framework for foodborne toxicity mitigation: a review

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ABSTRACT

Mycotoxins secondary metabolites from fungi such as *Aspergillus*, *Fusarium*, and *Penicillium* are widespread food contaminants that pose health risks, particularly in undernourished populations. Nutritional deficiencies and gut microbiota imbalances further compound their toxicity. This review explores the biochemical interplay among gut microbiota, dietary nutrients, and mycotoxin detoxification. A systematic review was conducted following PRISMA 2020 guidelines. Peer-reviewed studies published from January 2020 to March 2025 were retrieved from PubMed, Scopus, and Web of Science. Studies involving mycotoxins, gut microbiota, and nutritional modulation were included. Risk of bias was assessed using RoB 2 and PRISMA-ScR tools. Host phase I and II enzymes, along with microbial enzymatic systems, contribute to mycotoxin detoxification. Specific probiotic strains such as *Lactobacillus* and *Bifidobacterium* transform aflatoxins, ochratoxins, and trichothecenes into less toxic forms. Micronutrients like vitamins A, C, E, selenium, and polyphenols modulate detox pathways and redox balance. Prebiotics and polyunsaturated fats support microbial profiles favoring detoxification. Synergistic interventions, such as probiotic–prebiotic systems (PPSP), show promise in enhancing host resilience. The proposed gut microbiota–nutrition–mycotoxin triad offers a novel, integrative framework for mitigating foodborne toxicity. Understanding this biochemical cross-talk opens new avenues for precision nutrition, functional food development, and microbiome-targeted interventions aimed at reducing mycotoxin-induced health risks.

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1. Introduction

Mycotoxins are toxic secondary metabolites produced by fungi such as *Aspergillus*, *Fusarium*, and *Penicillium* that frequently contaminate food and agricultural commodities, particularly in humid environments. Major examples, including aflatoxins, fumonisins, and trichothecenes, have been associated with hepatocellular carcinoma, immune suppression, esophageal cancer, and gastrointestinal injury, and their effects are often worsened by nutritional deficiencies and gut microbiota imbalance in vulnerable populations (1).

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While nutrition, gut microbiota, and mycotoxin toxicity have each been studied independently, fewer works have examined their interaction within a unified mechanistic framework. This review therefore presents a triadic model linking nutritional modulators, gut microbiota, and mycotoxin detoxification, showing how diet can shape microbial detoxification capacity, how microbes can transform mycotoxins, and how mycotoxins can, in turn, impair nutrient absorption and disturb microbial balance (2).

The aim of this review is to clarify the biochemical crosstalk among gut microbiota, nutrition, and mycotoxins, and to explore how this relationship may be harnessed for improved food safety and health outcomes. It examines how nutritional status influences host and microbial detoxification pathways, how gut microbes biotransform mycotoxins, and how synergistic approaches such as probiotics, prebiotics, and precision nutrition may strengthen host resilience (3-5).

The gut microbiota functions as a dynamic biotransformation system capable of binding, sequestering, or enzymatically degrading mycotoxins, thereby reducing their toxic impact (6). Strains such as *Lactobacillus*, *Bifidobacterium*, and *Eubacterium* have shown detoxifying potential against aflatoxins and trichothecenes (6). However, prolonged mycotoxin exposure may disrupt microbial ecology, leading to dysbiosis, impaired nutrient absorption, and increased inflammation, with possible downstream effects on the gut–liver axis and systemic toxicity (7–10).

This diagram illustrates the bidirectional relationships between dietary nutrients, gut microbial composition, and mycotoxin metabolism. Nutrients influence microbial detoxification potential, while mycotoxins impair nutrient absorption and alter microbial balance.

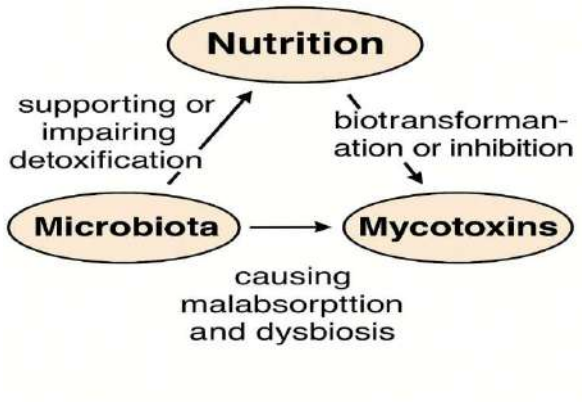

Figure 1. The gut microbiota–mycotoxin–nutrition triad [1-10].

2. Material and Methods

This review was conducted using rigorous and transparent systematic review methodology to collate peer-reviewed evidence on the biochemical interplay among mycotoxins, nutritional factors, and gut microbiota.

2.1. Search Strategy

A structured search strategy was applied across PubMed, Scopus, and Web of Science, targeting publications from January 2020 to March 2025. The strategy followed the PRISMA 2020 guidelines (11), and included search strings like: “mycotoxins and gut microbiota and nutrition” “aflatoxins and microbial detoxification” “nutrition and intestinal permeability and toxins”

All references were managed in EndNote, and screening was carried out in Rayyan QCRI (12). Search strategies were reviewed using the PRESS 2021 checklist (13).

2.2. Inclusion and exclusion criteria

Studies were included if they were published between 2020 and 2025 in English and peer-reviewed focused on interactions among mycotoxins, nutrition, and gut microbiota, designed as *in vitro*, animal, clinical, or systematic review/meta-analysis studies.

Exclusion criteria encompassed:

- Non-peer-reviewed articles (e.g., preprints, editorials).
- Studies without clear nutritional or microbial endpoints.
- Duplicate datasets.

Selection criteria and eligibility protocols were developed using the Cochrane Handbook (14), and scoped further using preferred report items for systematic reviews and meta-analyses extension for scoping reviews. PRISMA-ScR standards (15) and final inclusion parameters were defined following Cochrane Chapter 5 (16).

Risk of bias in randomized trials was assessed using Risk of Bias 2 Tool (RoB 2) (17), while non-randomized and mechanistic studies were evaluated following PRISMA 2020 methodology (18). Nutritional search parameters were informed by a recent systematic review of diet-diversity indicators (19). The protocol was dynamically updated using guidance for living systematic reviews (20).

Table 1 illustrates the structured protocol employed in section 2 to ensure a robust literature review process. It summarizes the tools and guidelines used for evidence screening, validation, and synthesis, emphasizing methodological rigor, transparency, and adaptability across toxicology, nutrition, and microbiota studies (11–20).

2.3. Study selection process

A structured study selection was carried out in line with preferred reporting items for systematic reviews and meta-Analyses 2020 (PRISMA 2020) guidelines to ensure transparency and reproducibility. Comprehensive searches were conducted across PubMed, Scopus, and Web of Science, and all retrieved records were screened using predefined inclusion and exclusion criteria. Studies were assessed for relevance to the triad of mycotoxins, gut microbiota, and nutritional modulation (11-20).

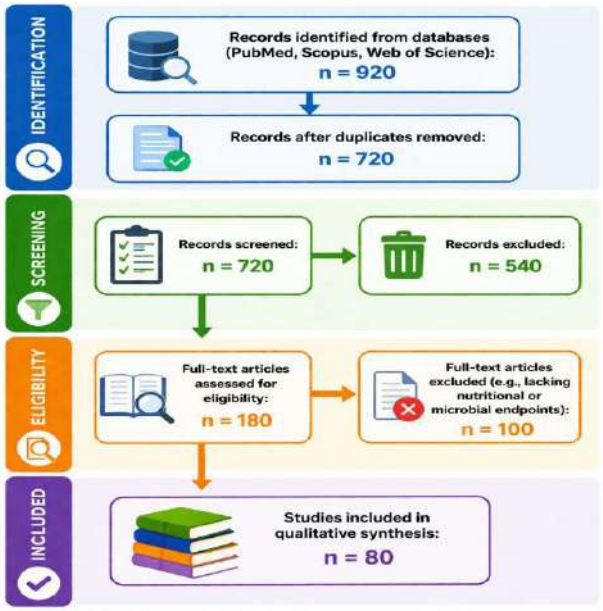

Figure 2. PRISMA flow diagram of study selection process [11-20]

This diagram summarizes the systematic review process from identification (n = 920) to final inclusion (n = 80). It outlines the number of records screened, excluded, and included according to PRISMA 2020 guidelines.

Table 1. Literature search and review framework

Component	Details	References
Review framework	Followed PRISMA 2020 protocol to ensure transparency and reproducibility	(11)
Screening tool	Rayyan QCRI used for independent blinded inclusion/exclusion review	(12)
Search validation	PRESS 2021 used to validate search string formulation and reduce retrieval bias	(13)
Review guidance	Cochrane Handbook 2022 used to shape eligibility and selection procedures	(14)
Scope definition	PRISMA-ScR methodology adopted to broaden inclusion of triad-relevant studies	(15)
Criteria development	Cochrane Chapter 5 guided operational definitions for inclusion/exclusion	(16)
Risk of bias (RCTs)	Assessed using RoB 2, tailored for randomized toxicology and nutrition studies	(17)
Reporting compliance	PRISMA 2020 compliance ensured comprehensive reporting across multiple study types	(18)
Nutritional search refinement	Diet-diversity frameworks refined keyword inclusion and relevance assessment	(19)
Dynamic protocol strategy	Living review methodology integrated to maintain temporal relevance and adaptability	(20)

Abbreviations: PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PRESS – Peer Review of Electronic Search Strategies; RoB 2 – Risk of Bias 2 Tool; ScR – Scoping Review

3. Results

This section presents the key findings of the review, showing how gut microbiota, dietary factors, and mycotoxin detoxification interact through microbial and host biochemical pathways. It also highlights the most promising protective mechanisms, current evidence gaps, and translational opportunities for reducing mycotoxin-related toxicity.

3.1. Biochemical pathways of mycotoxin metabolism

This figure summarizes phase I and phase II host enzymatic reactions and microbial degradation pathways involved in detoxifying dietary mycotoxins. It highlights oxidative, reductive, conjugation, and hydrolytic mechanisms, as well as the reconversion of masked toxins.

Thematic summary: Host and microbial enzymatic systems act in parallel to neutralize mycotoxins, with cytochrome P450 and UDP-glucuronosyltransferases (UGTs) driving host detoxification, while microbial esterases and probiotic enzymes break down toxins before systemic absorption.

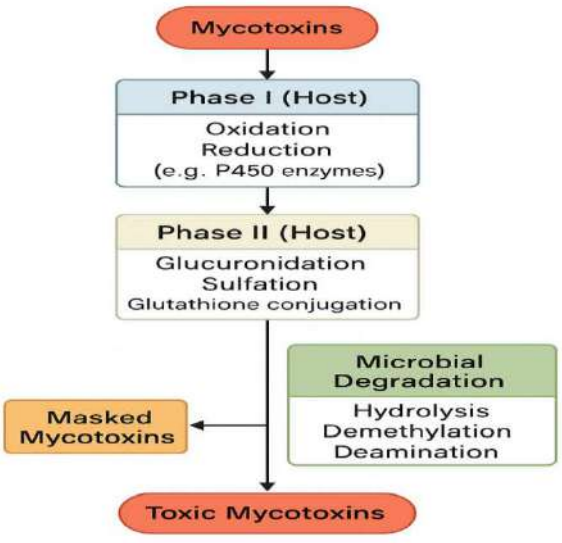

Figure 3. Schematic representation of mycotoxin metabolism pathways[21-30].

Table 2. Summary of microbial detoxification mechanisms of common mycotoxins

Microorganism	Mycotoxin targeted	Detoxification mechanism	Detoxified product	Citation(s)
Lactobacillus plantarum	Aflatoxin B_1	Enzymatic oxidation & binding	Non-toxic metabolites	(31)
Lactobacillus rhamnosus	Ochratoxin A	Peptidase-mediated hydrolysis	Ochratoxin α	(32)
Apiotrichum mycotoxinivorans	Zearalenone	Lactone ring cleavage	Non-estrogenic compound	(33)
Gut microbial esterases	Fumonisin B1	Tricarballylic acid side chain cleavage	Less toxic fumonisin backbone	(34)
Clostridium spp.	Masked mycotoxins	Reductive and hydrolytic cleavage	Non-toxic aglycones	(35)
Lactobacillus, *Bifidobacterium*	Multiple toxins	Multi-enzyme degradation	Various detoxified forms	(36,37)
PPSP systems	Emerging mycotoxins	Probiotic–postbiotic synergy detoxification	Food-grade detoxified products	(38)
Slackia, *Eubacterium*	Trichothecenes	De-epoxidation	Non-cytotoxic trichothecenes	(39)
Unclassified anaerobes	Zearalenone	Specific cleavage	Non-estrogenic metabolite	(40)

Abbreviations: OTA – Ochratoxin A; ZEN – Zearalenone; SCFA – Short-Chain Fatty Acids; PPSP – Probiotic–Postbiotic Synergy Platforms.

3.2. Microbial Detoxification Mechanisms

Table 2 illustrates microbial agents and enzymatic pathways responsible for transforming dietary mycotoxins into less or non-toxic derivatives. It supports the understanding of gut and probiotic detoxification capacities relevant to food safety.

3.3. Nutritional modulators of mycotoxin toxicity

Table 3 illustrates various nutrients and bioactive compounds that modulate host detoxification systems and gut microbial responses to dietary mycotoxins, These interactions promote health resilience through diverse mechanisms.

Thematic Summary: Gut microbes degrade diverse mycotoxins through enzymatic hydrolysis, ring cleavage, and de-epoxidation. These actions reduce toxicity and protect gut and liver function, especially when probiotic species are present.

3.4. Microbiota–nutrition synergy in mycotoxin resistance

Fig. 4 illustrates how dietary fibers and probiotics improve gut microbial composition, support epithelial integrity, and enhance immune detoxification of mycotoxins through short-chain fatty acid (SCFA) production and enzymatic transformation.

Table 3. Nutritional agents and their protective mechanisms against mycotoxins

Nutrient/Component	Mechanism of protection	Representative compounds	Citations
Functional foods	Nutrient repletion, microbial support	Fortified cereals	(41)
Dietary fiber	Adsorption, microbiota support, increased excretion	Inulin, β-glucans	(42)
Dietary fat	Alters microbial ecology, toxin uptake	Omega-3 PUFAs	(43)
Vitamins (A, B, C, E)	Enzyme modulation, antioxidant protection	Folate, ascorbate	(44)
Omega-3 fatty acids	Redox stabilization, anti-inflammatory effects	EPA, DHA	(45)
Vegan diets	Supports detoxifying microbiota, reduces toxin load	Fiber-rich plant foods	(46)
Minerals	Cofactor in antioxidant enzymes	Selenium, zinc	(47)
Polyphenols	Induce phase II enzymes, suppress toxin activation	Resveratrol, EGCG	(48)
Nutrient–microbiota–immunity Axis	Orchestrates systemic responses	Multi-nutrient synergy	(49)
Bioactive food compounds	Modulate gut microbial enzymatic activities	SCFAs, polyphenols	(50)

Abbreviations: EPA – Eicosapentaenoic Acid; DHA – Docosahexaenoic Acid; EGCG – Epigallocatechin Gallate; SCFA – Short-Chain Fatty Acids; PUFA – Polyunsaturated Fatty Acids.

Thematic Summary: Micronutrients, fibers, and polyphenols modulate detox enzymes, oxidative balance, and gut barrier function, thereby reducing systemic toxicity from ingested mycotoxins.

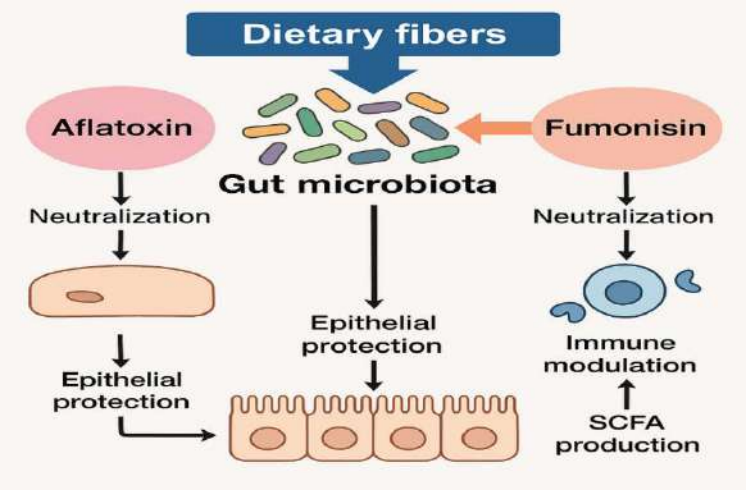

Figure 4. Mechanistic interaction between dietary fibers, probiotics, and gut microbiota in mycotoxin detoxification[51-60].

Table 4. Triadic interactions at a glance

Component	Influence on others	Outcome
Gut Microbiota	Metabolizes mycotoxins; influences nutrient absorption and immunity	Reduces toxin bioavailability; modulates host detox response
Nutrition	Shapes microbial diversity; regulates host detox pathways	Enhances microbial function and enzymatic detox
Mycotoxins	Disrupt microbiota; impair nutrient absorption and metabolism	Increases oxidative stress and toxin load

Thematic Summary: The synergistic effect of prebiotics, probiotics, and polyphenols enhances microbial resilience and toxin elimination. This integrated approach strengthens detoxification and supports immune-mucosal health.

Table 5. Summary of key research gaps in the gut microbiota–nutrition–mycotoxin interface

Gap category	Description	Citations
Mechanistic crosstalk	Undefined host–microbiome–toxin signaling pathways	(61)
In vivo human evidence	Few clinical or cohort studies evaluating real-life exposures	(62, 63)
Lack of multi-omics integration	Limited systems biology approaches in microbiome–toxin studies	(64)
Confounding by transit time	Uncontrolled gut transit variability affecting microbial and toxin dynamics	(65)
Masked mycotoxins	Unknown fate and toxicity of food-bound or transformed mycotoxins	(66)
Genetic polymorphisms	Underexplored role of host genotype in detox pathways	(67)
Nutrient–enzyme interactions	Poorly defined modulation of detox enzymes by dietary components	(68)
Functional food risk–benefit balance	Limited assessment of adverse vs. beneficial effects	(69)
Methodological standardization	No consensus on experimental protocols or metrics	(70)

Abbreviations: GST – Glutathione S-Transferase; UGT – UDP-Glucuronosyltransferase.

Table 6. Summary of evidence across study types

Focus area	Study type(s)	Strength of evidence	Key notes
Microbial detoxification of aflatoxins	*In vitro*, animal models	High	Multiple studies confirm enzymatic degradation
Nutrient modulation of ZEN and DON	Animal studies, human cohorts	Moderate	Antioxidant protection shown; limited human trials
Prebiotic-enhanced microbial function	*In vitro*	Moderate	SCFA production linked to gut resilience
Mycotoxin–microbiota–nutrient crosstalk	Reviews, mechanistic models	Conceptual	Emerging field; limited empirical validation
Genetic susceptibility (host)	Largely unexplored	Low	Detox enzyme polymorphisms remain underreported

Table 7. Translational strategies targeting mycotoxin detoxification pathways

Strategy	Target mechanism	Application domain	Citations
PPSP formulations	Microbiota modulation, xenobiotic metabolism	Human dietary supplements	(71)
Probiotic feed additives	Gut barrier enhancement, enzymatic degradation	Livestock industry	(72)
Clay/yeast detox blends	Physical adsorption of aflatoxins	Animal feeds	(73)
Enzymatic feed supplements	Direct mycotoxin hydrolysis	Monogastric/ruminant models	(74)
Synbiotic nutraceuticals	Microbial resilience, SCFA production	Functional food products	(75)
Personalized nutrition platforms	Diet-toxin matching via microbiome data	Digital health tools	(76)
Dietary fibers	SCFA stimulation, gut motility	Functional foods	(77)
AI-based dietary strategies	Real-time dietary optimization	Predictive nutrition systems	(78)
Bile acid modulation	Enhanced detox of lipophilic toxins	Microbial biochemistry	(79)
Mycotoxin-binding agents	Toxin sequestration in food matrices	Food safety technologies	(80)

Abbreviations: PPSP – Probiotic–Postbiotic Synergy Platforms; SCFA – Short-Chain Fatty Acids; AI – Artificial Intelligence.

Thematic Summary: Emerging strategies like PPSP systems, synbiotics, and AI-guided nutrition platforms offer real-world solutions for mycotoxin mitigation through microbiota and dietary engineering.

The illustration demonstrates how dietary components shape gut microbial composition to enhance detoxification. It emphasizes SCFA production, epithelial barrier support, and enzymatic neutralization of toxins.

3.4.1. Evidence quality and limitations

Table 4 presents a simplified synthesis of the triadic framework. It captures the dynamic interplay among gut microbiota, nutrition, and mycotoxins, highlighting their mutual influence and cumulative impact on health.

3.5. Gaps in current research

Table 5 illustrates the major limitations that need to be addressed to advance the field, including undefined host–microbiome–toxin crosstalk, limited human data absence of multi-omics integration and methodological inconsistencies.

To contextualize the strength and scope of available evidence supporting each component of the triadic model, Table 6 summarizes findings by focus area, study design, and evidence quality. This overview highlights where data are robust and where additional research is critically needed.

3.6. Potential for translational applications

Table 7 illustrates innovative strategies reshaping the detoxification landscape by leveraging gut microbiota dynamics and dietary modulation, including PPSP formulations, synbiotic nutraceuticals, personalized nutrition platforms and AI-driven optimization.

3. Discussion

This section interprets the findings in a broader scientific context, explaining how host enzymes, gut microbes, and nutritional modulators work together to influence mycotoxin metabolism. It also critically examines the limitations of current evidence and underscores the need for stronger human studies, multi-omics integration, and standardized methodologies.

The metabolism of mycotoxins within the host involves intricate phase I and phase II enzymatic reactions that either activate or detoxify these compounds (Figure 3). Phase I reactions, primarily catalyzed by cytochrome P450 monooxygenases, include oxidation, reduction, and hydrolysis, thereby increasing the polarity of mycotoxins (21). For instance, aflatoxins are hydroxylated in the liver to form more reactive intermediates such as aflatoxin B1-8,9-epoxide, which can bind to DNA and proteins (22). Similarly, *fumonisins* undergo deamination and hydrolysis as key phase I processes, ultimately yielding less toxic metabolites (23).

Phase II reactions, typically involving conjugation with glucuronic acid, sulfate, or glutathione, play a critical role in rendering mycotoxins more water-soluble and readily excretable (21,24). Zearalenone, a potent estrogenic mycotoxin, is extensively conjugated by UDP-glucuronosyltransferases (UGTs) and sulfotransferases in the liver and intestines, reducing its biological activity (25). Nutritional status, including micronutrient intake, can modulate phase II enzyme activity, influencing the rate and efficacy of detoxification (26).

However, recent comparative studies (e.g., Gerdemann et al.) have highlighted significant interspecies variability in cytochrome P450 activity and phase II conjugation. These findings challenge the reliability of animal models for predicting human metabolic responses to mycotoxins and underscore the need for human-specific enzyme kinetics data (22).

Beyond host metabolism, the gut microbiota contributes to the biotransformation of mycotoxins via microbial enzymes that can hydrolyze, reduce, or cleave chemical groups. Ochratoxin A, for example, is degraded by carboxypeptidases and microbial esterases into non-toxic derivatives such as ochratoxin α (27). Similarly, microbial metabolism has been shown to demethylate trichothecenes, mitigating their cytotoxic effects (28). Polymorphisms in cytochrome P450 genes have also been associated with interindividual variability in susceptibility to mycotoxin-induced toxicity (29).

Of particular concern are masked mycotoxins conjugated forms undetectable by standard analytical methods that can be hydrolyzed back into toxic parent compounds post-absorption (30). These masked forms challenge food safety assessments and require advanced metabolomic profiling for accurate quantification and risk evaluation.

The gastrointestinal microbiota plays a pivotal role in the degradation and detoxification of various mycotoxins, acting as a biochemical barrier that protects the host (Table 2). Several microbial genera, including *Lactobacillus*, *Clostridium, Bifidobacterium,* and *Apiotrichum*, are increasingly recognized for their enzymatic ability to transform or degrade toxic compounds into less harmful or non-toxic metabolites (31).

One of the best-characterized examples is the degradation of aflatoxins by bacterial species such as *Lactobacillus plantarum* and *Bacillus subtilis*, which metabolize aflatoxin B1 through enzymatic oxidation and binding mechanisms (31). Similarly, *Lactobacillus rhamnosus* strains have shown the ability to degrade ochratoxin A (OTA), converting it into ochratoxin A via peptidase-mediated hydrolysis (32).

In addition to bacteria, certain yeast species such as *Apiotrichum mycotoxinivorans* have demonstrated significant detoxification potential. These organisms degrade zearalenone (ZEN) via lactone ring cleavage, rendering it non-estrogenic (33). This fungal detoxification capacity is paralleled by gut microbial enzymes that act on fumonisins, especially by cleaving the tricarballylic acid side chains, as shown by recent discoveries of novel microbial carboxylesterases (34).

Clostridium species also participate in the biotransformation of masked mycotoxins through reductive and hydrolytic cleavage mechanisms, offering an anaerobic pathway of detoxification particularly relevant in the colon (35). These reactions are supported by multi-enzyme systems expressed in situ by gut microbes and influenced by host diet and microbial composition (36).

Nevertheless, much of the existing evidence is derived from in vitro models with simplified microbial communities and do not reflect the full ecological complexity of the human gut. This limitation has been pointed out by recent systematic reviews (Lázaro et al.), which call for more well-controlled human or animal studies to validate detoxification efficiency under realistic conditions (6).

Recent integrative reviews have mapped the molecular landscape of microbial detoxification, highlighting synergistic interactions among probiotic strains, especially *Lactobacillus* and *Bifidobacterium*, in degrading a spectrum of mycotoxins, including fumonisins, trichothecenes, and ZEN (36,37). Moreover, probiotic and postbiotic systems referred to as PPSP (probiotic–postbiotic synergy platforms) are

being explored for functional food development targeting mycotoxin mitigation (38).

Bacterial strains such as *Slackia* and *Eubacterium* have been found capable of de-epoxidizing trichothecenes, a critical step that neutralizes their cytotoxic activity. These transformations are often enabled by oxygen-independent enzymes, making them highly suitable for the anaerobic gut environment (39). Lastly, bioconversion of ZEN into non-estrogenic metabolites by Sun et al. confirmed the specificity and efficiency of microbial cleaving reactions (40).

The toxicity of mycotoxins can be significantly modulated by dietary components including vitamins, minerals, antioxidants, and dietary fibers, which influence host detoxification pathways and microbial balance. These modulatory effects operate via gut microbiota dynamics, redox signaling, and enhancement of metabolic defenses (Table 3).

Functional foods enriched with vitamins and minerals have been increasingly recommended to counteract micronutrient deficiencies that exacerbate the toxic effects of mycotoxins. However, such enrichment must be approached cautiously due to potential interactions between certain nutrients and toxin absorption mechanisms (41).

Dietary fiber plays a critical role in limiting mycotoxin bioavailability by forming physical complexes that impede absorption and by nourishing gut microbes that can degrade or bind mycotoxins (42). Specifically, soluble fibers such as inulin, β-glucans, and arabinoxylans have been associated with increased fecal excretion of mycotoxins (42).

Dietary fat intake also shapes gut microbial composition, which in turn affects mycotoxin metabolism and immune modulation. High-fat diets may enhance lipophilic toxin absorption, whereas polyunsaturated fats like omega-3 fatty acids support microbial taxa that promote detoxification (43).

Micronutrients such as vitamins A, C, E, and B-complex vitamins are known to regulate xenobiotic metabolism. For example, they upregulate detoxification enzymes like cytochrome P450s and Glutathione-S-transferases involved in mycotoxin clearance (44). These vitamins also protect against mycotoxin-induced oxidative stress, which underlies tissue injury and immune suppression.

However, inconsistencies remain across different studies. For example, Panda et al. reported upregulation of detoxification enzymes in response to vitamin C and E supplementation (26), whereas Paduchová et al. found minimal effect in aged animal models (45). These discrepancies highlight the importance of context age, baseline nutrient status, and toxin type in interpreting micronutrient efficacy.

Omega-3 fatty acids especially EPA and DHA reduce lipid peroxidation, mitochondrial damage, and inflammation triggered by mycotoxins such as aflatoxin B1 and Zearalenone. Their mechanisms involve attenuation of NF-κB signaling and preservation of cellular redox balance (45).

Plant-based diets, especially vegan regimens, are associated with a beneficial gut microbial composition that supports mucosal integrity and diminishes the enterohepatic circulation of toxins. The predominance of fiber and polyphenols in such diets enhances microbial fermentation, which may lead to toxin degradation or entrapment (46).

Minerals like selenium and zinc serve as cofactors for antioxidant enzymes such as glutathione peroxidase and superoxide dismutase. Supplementation has shown protective effects against the immunotoxic and hepatotoxic effects of trichothecenes and fumonisins (47).

Polyphenols, a class of dietary antioxidants, can induce phase II detoxification enzymes, reduce inflammation, and inhibit bioactivation of aflatoxins through modulation of aryl hydrocarbon receptors and Nrf2 pathways (48).

The nutrition–microbiota–immunity axis highlights the systemic influence of dietary components. Nutrients modulate microbial communities, which in turn influence immune responses and gut-liver communication, critical during mycotoxin exposure (49).

Recent advances underscore the ability of various food-derived compounds to reshape microbial enzymatic activities. Polyphenols, vitamins, and short-chain fatty acids produced from fiber fermentation exhibit synergistic effects in reducing mycotoxin-related damage (50).

The synergy between gut microbiota and dietary intake plays a pivotal role in modulating host resistance to mycotoxins. Through complex host-microbe interactions, specific nutrients and dietary patterns can modulate the gut microbial composition and functionality, thereby enhancing mycotoxin detoxification (Figure 4).

Recent studies demonstrate that probiotics, prebiotics, synbiotics, and postbiotics (PPSP) collectively contribute to the attenuation of mycotoxin toxicity via mutual detoxification mechanisms. For example, targeted prebiotics, probiotics, synbiotics and postbiotics (PPSP) interventions have shown substantial mitigation of zearalenone and aflatoxin effects by boosting microbial enzymatic activity and barrier integrity (51).

Nutritional elements, particularly dietary fibers and polyphenols, are shown to remodel gut microbial ecosystems towards a detoxification-prone phenotype. Fermentable fibers can elevate beneficial taxa like *Bifidobacteria* and *Lactobacillus* spp., which secrete enzymes capable of binding or degrading mycotoxins (52,53). These alterations also modulate short-chain fatty acid production, which indirectly improves mucosal immunity and hepatic detox responses (54).

Moreover, case studies involving human and animal trials illustrate that diet-induced modulation of gut microbiota profoundly impacts systemic resistance to mycotoxins. For instance, dietary fiber-enriched regimens increased fecal excretion of ochratoxin and zearalenone in rats, likely due to enhanced microbial fermentation (55). Similarly, probiotics such as Lactobacillus strains have been documented to detoxify ochratoxin A in food matrices and *in vivo* models (56).

These observations are supported by Cosier et al., who, in a recent meta-analysis, found significant reductions in OTA levels and gut inflammation markers among subjects receiving PPSP supplementation (51). However, they also emphasized the variability in outcomes depending on probiotic strain, prebiotic type, and host baseline microbiota.

Beyond individual interventions, the host-microbe-nutrition triad is essential for systemic resilience against toxin insult. Gut microbiota not only metabolizes mycotoxins but also communicates with immune and epithelial systems through microbial metabolites. Clinical frontier research reveals how

nutrient-guided modulation of the microbiome can be harnessed for precision detox therapy (57).

Emerging evidence also supports the use of prebiotic fibers to enhance fecal elimination of trichothecenes and fumonisins. Prebiotic-rich diets promote the expansion of butyrate-producing Firmicutes, which upregulate detoxification pathways and maintain gut barrier function (58). These effects are further amplified in synbiotic formulations, where probiotic strains and fermentable substrates act synergistically (59). Notably, gut bacteria-derived enzymes continue to gain attention for their specificity in degrading fumonisin and aflatoxin variants (60).

While this review synthesizes a growing body of literature linking gut microbiota, nutrition, and mycotoxin detoxification, the overall quality of evidence varies considerably. A critical appraisal using the Risk of Bias 2 (RoB 2) tool and adapted PRISMA-ScR protocols revealed several recurring limitations.

Many included studies were preclinical (animal or *in vitro*), with limited generalizability to human populations. Additionally, heterogeneity in study design, outcome measures, and microbial taxa examined made direct comparisons difficult. Some mechanistic studies lacked proper controls, and few quantified dose–response relationships or conducted long-term follow-up.

Moreover, the reporting quality in several clinical studies was inconsistent, especially regarding blinding, sample size justification, and statistical adjustments for confounders. These limitations suggest that while findings are promising, they should be interpreted with caution, and future research must emphasize methodological rigor and standardization to support translational applications.

To consolidate the integrated biochemical relationships explored across microbial detoxification, nutritional modulation, and host–toxin interactions (Table 4).

Despite mounting evidence linking gut microbiota, dietary factors, and mycotoxin biotransformation, several key research gaps remain unresolved. These limitations hinder translational progress toward personalized nutrition-based mycotoxin mitigation strategies (Table 5).

One prominent gap is the lack of mechanistic understanding regarding host–microbe–toxin crosstalk. Although various studies suggest that microbial metabolites interact with host detoxification pathways, the molecular signaling networks and receptor-level interactions remain poorly characterized (61). Without such clarity, interventions remain empirical rather than precision-based.

Another significant limitation lies in the scarcity of human in vivo studies. Many studies included in existing reviews (e.g., Fan et al.) rely heavily on rodent data with limited translatability to human gut-microbiome interactions. Even within these, strain-specific effects are inconsistently reported, and studies rarely incorporate long-term dietary patterns or real-world exposure levels (57).

Much of the available data is derived from rodent models or in vitro systems, which do not fully capture the complexities of human gastrointestinal dynamics, interindividual microbiota variability, and immune-metabolic interplay (62). Even recent analyses of PPSP strategies remain largely qualitative, often lacking

quantitative dose–response or systems biology interpretations (63).

The advent of multi-omics approaches (e.g., metabolomics, metagenomics, proteomics, and transcriptomics) offers unprecedented resolution in dissecting host–microbiota–toxin interactions. However, such integrative analyses are underutilized in current studies, particularly in nutritional toxicology and mycotoxin research (64).

A notable methodological challenge includes gut transit time, which is increasingly recognized as a major confounding variable in microbiota research. It affects microbial composition, fermentation efficiency, and nutrient absorption, all of which influence toxin metabolism (65). These factors are often not adequately controlled or reported.

The fate of masked mycotoxins metabolites bound to food matrices or transformed by microbes is another underexplored area. Their bioavailability, toxicokinetics, and long-term health effects remain largely unknown, despite their growing dietary prevalence (66).

Genetic polymorphisms in both host detoxification genes and microbial enzymes further add layers of complexity. Individual variation in GST, UGT, or cytochrome P450 isoforms may modulate susceptibility to mycotoxins and response to dietary interventions, yet few studies address this variability (67).

Moreover, the interplay between nutrients and mycotoxin-detoxifying enzymes such as phase I and II biotransformation enzymes is insufficiently characterized. While vitamins, minerals, and polyphenols are known to modulate these enzymes, the directionality, dose thresholds, and synergistic effects remain unclear (68).

Functional foods designed to reduce toxin exposure often lack rigorous benefit–risk evaluations. Some may inadvertently alter microbial resilience or enzyme expression in undesirable ways (69).

Finally, there is a lack of standardized protocols across studies (table 6). Heterogeneity in sample collection, microbial analysis, mycotoxin quantification, and statistical interpretation compromises reproducibility and cross-study comparisons (70).

The convergence of microbiome research, dietary science, and toxicology has paved the way for diverse translational applications aimed at mitigating the adverse effects of mycotoxins. These innovations span from probiotic and prebiotic formulations to precision nutrition platforms and advanced feed detoxification strategies, underscoring the shift from reactive food safety to proactive nutritional toxicology (Table 7).

One of the most promising interventions lies in the development of (PPSP) strategies. These compounds enhance microbial resilience and modulate host detoxification pathways, thereby reducing mycotoxin bioavailability and toxicity. Although PPSP approaches are still emerging, recent findings show they can modulate key gut microbial populations involved in xenobiotic metabolism, particularly under simulated gastrointestinal conditions (71).

However, existing PPSP interventions vary widely in formulation and study design, limiting direct comparison across trials. Smolinska et al. noted a lack of standardization in strain selection, dosage, and endpoint measurement, which complicates translation into regulatory frameworks and clinical guidelines (72-76).

Probiotic feed additives, particularly those used in livestock, represent a mature and scalable application.

Supplementation with strains such as *Lactobacillus*, *Bacillus*, and *Enterococcus* not only improves gut barrier integrity but also enhances enzymatic degradation of mycotoxins, leading to improved animal health and reduced toxin carryover into human food products (72). When combined with clay minerals and yeast cell wall derivatives, the efficacy of these feed interventions improves substantially. These composites physically bind aflatoxins and reduce their intestinal absorption, representing a cost-effective biophysical detoxification route (73).

At the molecular level, enzymatic detoxification agents, such as carboxylesterases and epoxide hydrolases, are increasingly formulated into feed supplements. These enzymes hydrolyze mycotoxins into non-toxic derivatives and have demonstrated efficacy in both monogastric and ruminant models (74). As natural complements, synbiotic nutraceuticals comprising probiotics and fermentable fibers have shown dual functionality: restoring microbial balance and enhancing enzymatic detoxification capacity (75).

In the human domain, personalized nutrition platforms represent a significant translational frontier. Leveraging individual microbiome profiles, these tools tailor dietary regimens that either reduce dietary mycotoxin intake or enhance detoxification capacity. Integration with wearable biosensors and machine-learning algorithms further refines the precision of such interventions (76).

Dietary fibers, especially resistant starches and inulin, contribute to mycotoxin detoxification by promoting short-chain fatty acid (SCFA) production and gut motility, which accelerates toxin clearance (77). Furthermore, AI-powered decision-support systems are now being deployed to optimize dietary plans based on toxin exposure risk, microbiome data, and nutrient interactions (78). These platforms hold promise for community-wide nutritional surveillance and risk mitigation.

Emerging data also suggest that bile acid metabolism can modulate gut microbial detoxification of lipophilic mycotoxins. Targeting bile acid pools via diet or probiotics may offer an indirect but effective detoxification mechanism (79). Finally, mycotoxin-binding agents incorporated into food matrices and packaging materials are gaining traction. These agents often derived from silicates, activated carbon, or biopolymers immobilize toxins before they are absorbed, offering an exogenous layer of defense (80).

5. Conclusion

This review highlights the intricate biochemical interplay between gut microbiota, dietary nutrients, and mycotoxin metabolism, framing a triadic model for mitigating foodborne toxicity. Host and microbial enzymatic systems, particularly Phase I and II pathways, work in concert with dietary modulators to neutralize mycotoxins. Probiotics, prebiotics, and micronutrients not only enhance detoxification efficiency but also restore gut microbial balance and barrier integrity. Emerging evidence supports the potential of synergistic probiotic and prebiotic systems and personalized nutrition platforms in reducing toxin burden. However, translational challenges persist, including limited human trials, underutilization of multiomics approaches, and poorly defined nutrient and enzyme interactions. Addressing these gaps is critical to advancing precision nutrition strategies for food safety and public health resilience.

Significant statement

This manuscript provides a comprehensive synthesis of the biochemical interactions between gut microbiota, dietary nutrients, and mycotoxins. It emphasizes how nutritional modulation can enhance microbial detoxification pathways while mitigating the adverse effects of dietary toxins. By integrating insights from enzymology, microbiology, and nutritional science, the study proposes a triadic framework for food safety intervention. The work highlights the promise of probiotic and prebiotic strategies in restoring gut integrity and reducing toxin burden. It also underscores the need for translational research and multiomics integration. This contribution is timely and impactful for advancing precision nutrition and toxicology.

Type of article

Abbreviations

OTA – Ochratoxin A

ZEN – Zearalenone

DON – Deoxynivalenol

SCFA – Short-Chain Fatty Acid

EPA – Eicosapentaenoic Acid

DHA – Docosahexaenoic Acid

GST – Glutathione S-Transferase

UGT – UDP-Glucuronosyltransferase

PPSP – Probiotic–Postbiotic Synergy Platforms

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

RoB 2 – Risk of Bias 2 Tool

PRISMA-ScR – PRISMA Extension for Scoping Reviews

PRESS – Peer Review of Electronic Search Strategies

AI – Artificial Intelligence

NF-κB – Nuclear Factor Kappa-light-chain-enhancer of Activated B Cells

AEM – Applied and Environmental Microbiology

JAF – Journal of Agricultural and Food Chemistry

EGCG – Epigallocatechin Gallate.

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Author contributions

Both authors contributed equally to the conceptualization, methodology, literature collection, analysis of the reviewed studies, manuscript drafting, and final approval of the submitted version. david chinonso anih served as the corresponding author.

Declaration of competing interest

The authors declare that they have no conflicts of interest related to this manuscript. There are no personal, financial, or professional interests that influenced the preparation of this systematic review.

Data availability

Data are available on demand.

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