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Recent advances in the biosynthetic mechanisms, regulation, and detoxification strategies of deoxynivalenol in *Fusarium graminearum*

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Fusarium graminearum, the major causal agent of Fusarium head blight (FHB), produces the trichothecene mycotoxin deoxynivalenol (DON), which threatens food and feed safety worldwide. This review synthesizes recent advances in DON biosynthesis, emphasizing the *TRI* gene cluster and its pathway enzymes, transcriptional regulators, and signaling cascades. In parallel, it provides a comprehensive analysis of the molecular mechanisms involved in regulating DON biosynthesis, with a focus on the *TRI* cluster. In additionally, current progress in detoxification strategies is summarized, covering physical, chemical, and biological methods aimed at mitigating DON contamination in food and feed. This review further explores the endogenous environmental factors influencing DON synthesis and offering insights to the development of integrated control strategies against DON contamination. By integrating the current findings, this review aims to support the development of effective strategies, control *F. graminearum* and mitigate FHB.

KEYWORDS

Fusarium head blight, deoxynivalenol (DON), TRI gene cluster, biosynthesis, regulation, detoxification

1 Introduction

Fusarium graminearum is the primary fungal pathogen responsible for FHB in wheat, a disease that threatens global grain yields and food safety (1, 2). A major concern associated with *F. graminearum* is the production of deoxynivalenol (DON) (Figure 1), or “vomitoxin,” a mycotoxin that contaminates wheat and other cereals, which poses risks to the human and animal health (3, 4). Based on the recent reports, DON is one of the most common food-related mycotoxins in the world (5). Acetylated derivatives of deoxynivalenol (DON), mainly 3-ADON and 15-ADON, act as DON precursors with slightly reduced toxicity, regulated by *FgTRI8* (6). Pathogen subspeciation has diversified their production. Deoxynivalenol-3-glucoside (D3G), a masked DON derivative, can hydrolyze *in vivo* to DON, intensifying toxicity (7). According to the Food and Agriculture Organization (FAO), approximately 25% of global food crops are contaminated with mycotoxins annually, which causes economic losses of over USD 100 billion (8, 9).

China, as one of the world's largest wheat producers, is particularly vulnerable to FHB (10). The disease affects millions of hectares of wheat annually, with the outbreak potentially resulting in unprecedented yield losses of the nation's wheat production (11–13). This review

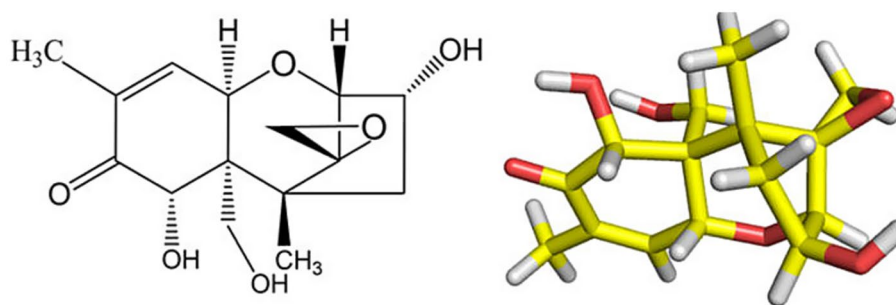


FIGURE 1

The chemical structure and stereochemical structure of DON. Key functional groups (epoxide, C9–C10 double bond) that underlie toxicity and guide detoxification chemistry are indicated.

integrates these advances to (i) map DON biosynthesis and its regulation from gene to environment, and (ii) compare detoxification strategies with an emphasis on mechanisms, limitations, and translational prospects for integrated FHB management.

1.1 Geographic distribution and impact

F. graminearum is widely distributed across humid and semi-humid regions, with particularly high incidence in the temperate zones, including the Yangtze River Basin in China, the Great Lakes region of North America, and Central Europe (14–16). It infects over 30 cereal crops, including wheat, barley, maize, and oats (17–19).

According to the Biomin Global Mycotoxin Survey (Figure 2), East Asia, North America, and Europe experience the highest levels of DON contamination (20). Across the world, FHB had caused an estimated loss of over \$10 billion (21). Similarly, the reported incidence of DON contamination was very high across different regions, with 94% in America and China and 77% in Europe (22, 23). DON and its acetylated derivatives exert detrimental effects on the human health, which could lead to a severe FHB outbreak and reduced wheat yields, potentially leading to multiple cases of livestock poisoning from DON exposure (24). Contamination levels of 3-ADON and 15-ADON are strongly correlated, and their co-occurrence produces synergistic toxicity. Studies show that baking degrades DON acetylated derivatives (25), while Juan-García et al. (26) demonstrated their cytotoxicity and metabolic products in HepG2 cells. Ozone treatment can also degrade DON, with degradation byproducts exhibiting negligible toxicity (Sun et al.) (27).

In China, FHB is most prevalent in the humid and rainy region of Yangtze River Basin, with its distribution expanding northward (28). The annual yield losses in the middle and lower Yangtze River region typically range from 10 to 15%, with severe outbreaks reducing the yields by up to 50% (29, 30). One of the earliest large-scale outbreaks occurred in Henan Province in 1985, which affected 3 million hectares of wheat fields (31). Since 2000, climate change and shifts in the cultivation practices have intensified the spread of FHB (32). Approximately 80% of wheat crops across China were contaminated to varying degrees, causing a decline in the national grain production decline of >20% (31, 33, 34). This wheat-maize rotation system has contributed to the persistence of *F. graminearum*, with Henan and Shandong Provinces emerging as high-risk areas (35).

1.2 Disease cycle

The *F. graminearum* comprises of the following four key stages: overwintering, spore release, infection, and secondary spread (36, 37) (Figure 3).

Regions with recurrent high DON incidence (East Asia, North America, Europe) are highlighted.

1.2.1 Overwintering

Following harvest, *F. graminearum* persists as a saprophyte on crop residues, including grains and stalks, producing both mycelia and perithecia that facilitate infection in subsequent seasons (19, 38, 39). Vegetative mycelia, which is responsible for nutrient absorption, can survive on the soil surface for up to 1 year or for 1–2 months when buried (19). Dormant perithecia remain viable at soil temperatures greater than -20°C (40).

1.2.2 Spore release

In spring, when temperatures reach approximately 10°C and the relative humidity is >80%, perithecia mature and release large quantities of ascospores and conidia under moist conditions (41, 42). Air currents and rain splash facilitate spore dispersal to wheat spikes, which initiate infection.

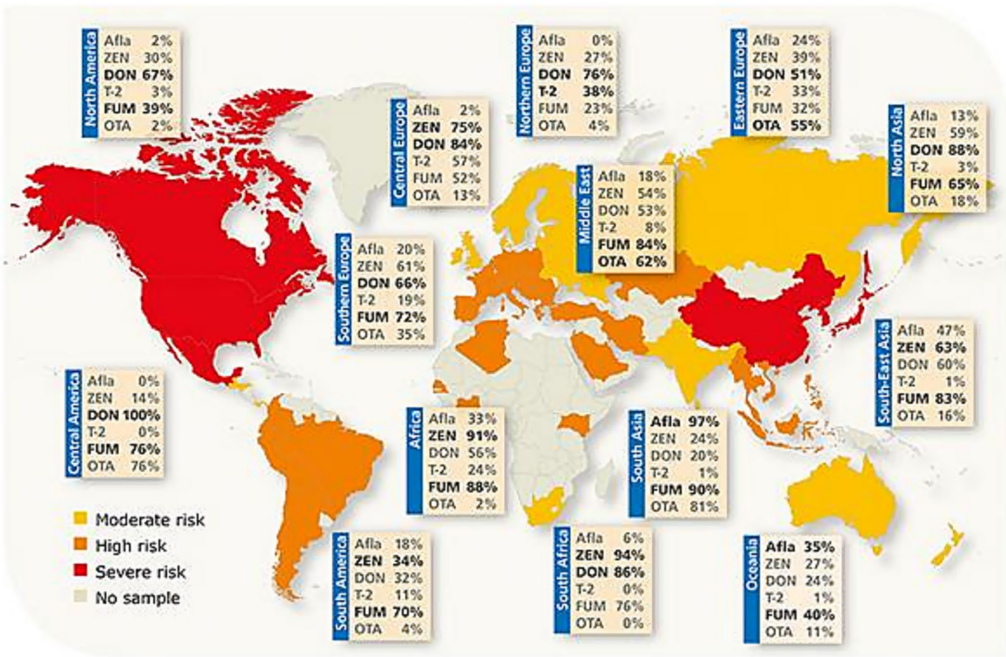
1.2.3 Infection

Upon reaching wheat spikes, *F. graminearum* ascospores and conidia, forming hyphae that initially infect the anthers before spreading into the glumes and spikelets (43, 44). The infected tissues develop water-soaked brown lesions, and the fungus colonizes the spike through the rachis (45). Under warm and humid conditions, the infected spikes turn pale-yellow or white, often displaying characteristic pink or brownish fungal masses (46).

1.2.4 Secondary spread

Ascospores and conidia produced on infected plants can cause secondary infections in late-season wheat crops or in the adjacent summer maize fields (47). These spores may also form perithecia on crop residues, allowing *F. graminearum* to overwinter and contribute to primary infections in the following planting season (48).

Under dry conditions, *F. graminearum* may enter a latent phase, temporarily halting its spread and symptom development (49). However, increased moisture can reactivate this disease, often causing



The latest survey compiles the results of more than 30,000 analyses to give an overview of the main threats caused by the six main agricultural relevant mycotoxin groups including aflatoxins (Afla), zearalenone (ZEN), deoxynivalenol (DON), T-2 toxin (T-2), fumonisins (FUM) and ochratoxin A (OTA).

FIGURE 2
Distribution of mycotoxin contamination in the world.

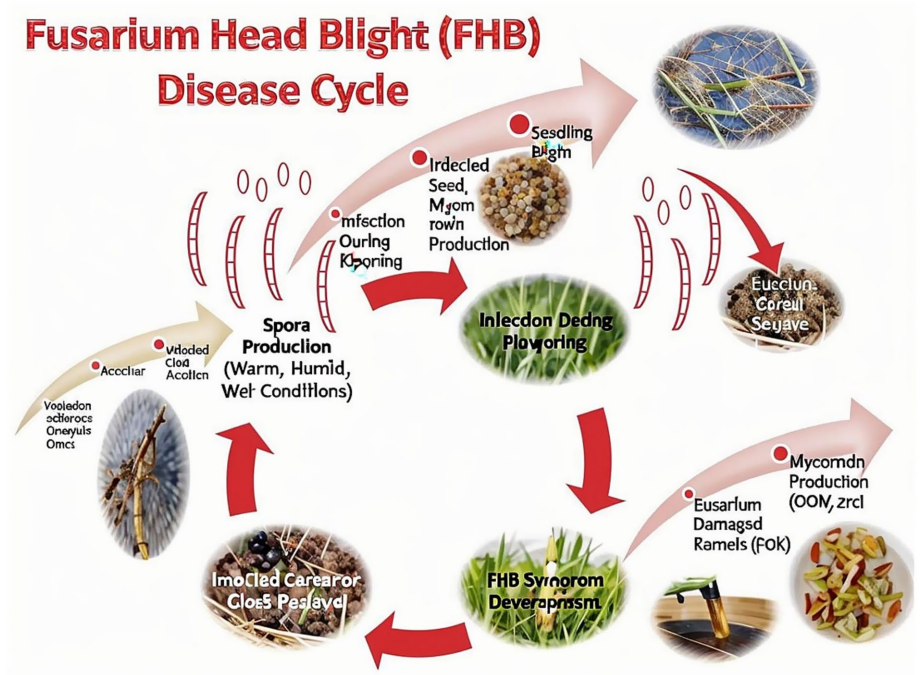


FIGURE 3
The cycle of *Fusarium graminearum* infection. Overwintering on residues, ascospore/conidial release, floret infection, and secondary spread are summarized with environmental triggers (temperature, humidity; cite from <https://www.saskatchewan.ca/business/>).

severe epidemics (50). This observation underscores the importance of overwintering inoculum and perithecia formation in sustaining *F. graminearum* populations (19). The interplay between favorable weather conditions, abundant inoculum sources, and continuous wheat cultivation drives the recurrent nature of FHB outbreaks (51).

2 Biosynthesis and molecular mechanism of DON

The biosynthesis of DON is regulated by a coordinated enzymatic network encoded by the *TRI* family (52). All *TRI* involved in DON biosynthesis in *F. graminearum* have been identified, which includes nearly 10 core *TRI*, along with *TRI101* and *TRI1* through *TRI16* (Figure 4). The roles of these genes in DON biosynthesis have been largely elucidated, thereby clarifying the overall biosynthetic pathway (Figure 5).

Among these genes, *TRI1* encodes a C-8 hydroxylase, whereas *TRI3* encodes an acetyltransferase (53). *TRI4* encodes a cytochrome P450 monooxygenase, and *TRI5*, also known as the trichodiene synthase gene, catalyzes the initial step in trichothecene biosynthesis (54). *TRI6* and *TRI10* function as the key regulatory genes, controlling both trichothecene biosynthesis and the expression of other *TRI* genes (55). Specifically, *TRI6* acts as a self-regulated transcription factor that modulates the *TRI10* expression through promoter binding (56). *TRI7* and *TRI13* together determine the specific chemical type of DON produced (57). Meanwhile, *TRI8* encodes a deacetylase, and *TRI12* encodes a transporter protein that serves as an efflux pump for trichothecene toxins (58, 59).

The biosynthesis process begins with the cyclization of farnesyl pyrophosphate (FPP) into the non-toxic intermediate trichodiene, catalyzed by trichodiene synthase (*TRI5*). This step is the first and most critical in DON biosynthesis. Trichodiene is subsequently hydroxylated at the C2 position, epoxidized between C12 and C13, and hydroxylated at C11 and C3 by the cytochrome P450 monooxygenase (*TRI4*), resulting in the formation of the intermediate iso-trichotriol (60, 61).

Iso-trichotriol then undergoes two non-enzymatic isomerization steps, shifting the hydroxyl group from C9 to C11 (7). A covalent bond subsequently forms between the oxygen atoms at C2 and C11, yielding iso-trichodermol, the core structure of trichothecene toxins (62). Iso-trichodermol is then acetylated at C3 by the acetyltransferase *TRI101*, forming 3-acetyl-iso-trichodermol (63). Hydroxylation at

C15, catalyzed by the *TRI1*-encoded hydroxylase, produces 15-deacetylcalonecetrin (54, 64). This intermediate product is further acetylated at C15 by the acetyltransferase *TRI3*, forming calonecetrin (65). Additional hydroxylation at C7 and C8, followed by the conversion of the C8 hydroxyl group into a keto group, results in the formation of either 3-acetyldeoxynivalenol (3-ADON) or 15-ADON, depending on the substrate specificity of the *TRI8*-encoded deacetylase. The final deacetylation step yields DON (66).

As the *TRI* family directly controls DON biosynthesis, the expressions of *TRI* are central to the regulation of toxin production (67). *TRI5* was the first toxin biosynthesis gene identified and cloned in *F. graminearum*. Functional studies have demonstrated that deletion of *TRI5*, which significantly reduces the pathogenicity of *F. graminearum*, while reintroducing the wild-type gene restores both toxin production and pathogenicity (67). These gene complementation experiments not only confirmed the essential role of *TRI5* in the biosynthetic pathway but also underscored its critical position within the broader regulatory network (68).

The transcription factor *TRI6* serves as a key regulator, functioning alongside *TRI10* to control the expression of other *TRI* genes (69). Microarray analyses have demonstrated that the deletion of *TRI6* or *TRI10* affects the expression of > 50% of *TRI* genes, including *TRI12*, which encodes the toxin efflux pump (67). Beyond regulating *TRI* genes, *TRI6* and *TRI10* also influence genes involved in the mevalonate pathway, such as HMR1, which encodes 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase), as well as genes associated with isoprenoid precursor synthesis, including those responsible for FPP production (55). The loss of *TRI6* significantly downregulates the expression of *TRI3* and *TRI4*, further disrupting DON biosynthesis (52). In addition, *TRI14* has been identified as an important regulatory gene influencing DON accumulation.

Although DON biosynthesis follows a stepwise process, it occurs within a complex metabolic network, where the sequence of individual reactions is not strictly linear (62, 70).

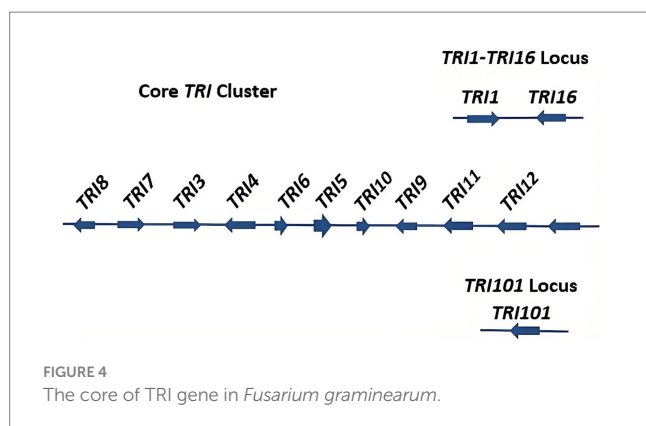
3 Regulatory mechanisms of DON biosynthesis

The regulation of DON biosynthesis is governed by both endogenous signaling pathways and external environmental factors (71, 72).

3.1 Regulation of DON biosynthesis by endogenous signaling pathways

Several cellular signaling pathways also contribute to the regulation of DON biosynthesis, including the mitogen-activated protein kinase (MAPK) pathway, the cyclic AMP-protein kinase A (cAMP-PKA) pathway, and the Target of Rapamycin (TOR) pathway (69).

The MAPK pathway regulates DON production through three phosphorylation cascades: Mgv1, Gpmk1, and FgHog1 (67). The deletion of core kinases in the Mgv1 pathway (i.e., FgBck1, FgMmk2, FgMgv1) severely impairs pathogenicity, restricts fungal spread to the initial infection site, and almost completely eliminates DON production (73). In the Gpmk1 pathway, the deletion of



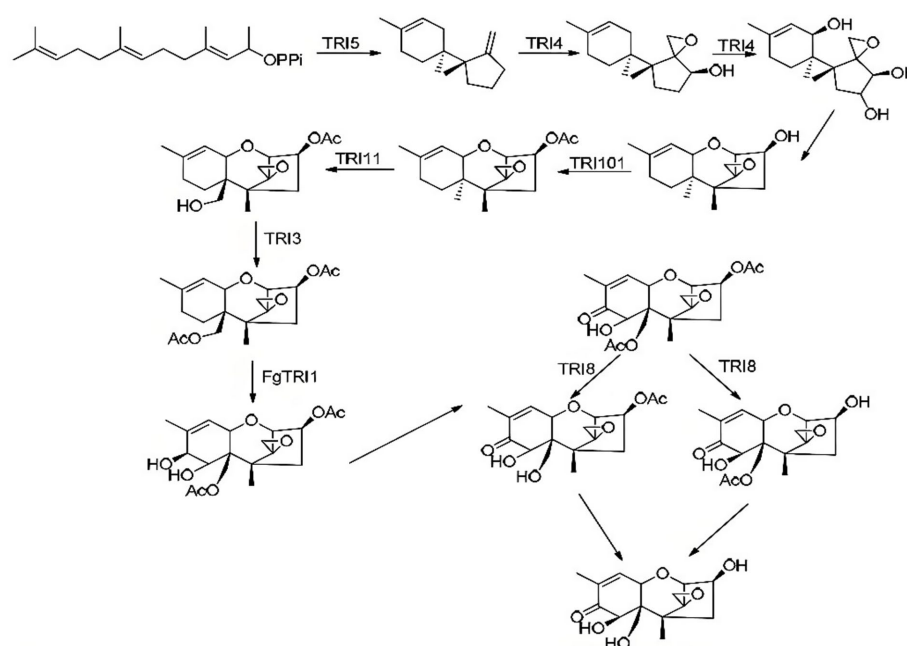


FIGURE 5

The biosynthetic pathway of DON in *Fusarium graminearum*.

FgSte11, FgSte7, or Fgpmk1 significantly reduces both the colonization ability and DON production in wheat spikes. Similarly, the disruption of the osmotic stress-pathway genes FgHOG1, FgPBS2, and FgSSK2 significantly inhibits DON biosynthesis (13).

The cAMP-PKA pathway regulates DON biosynthesis through the catalytic subunit gene FgCPK1 and the adenylate cyclase gene FgFAC1 (74). The deletion of FgCPK1 reduces the DON production, whereas the deletion of FgFAC1 completely abolishes DON biosynthesis (74–76).

The TOR pathway influences DON biosynthesis through FgTOR1/2, which encode the only kinases in this pathway and through the Tap42 complex genes (i.e., FgPP2A, FgSIT4, and FgPPG1). Among these, only the deletion of FgPPG1 could completely block DON biosynthesis (77, 78).

3.2 The influence of the external environment on DON biosynthesis

Environmental factors such as temperature, humidity, pH, carbon and nitrogen sources, hydrogen peroxide (H_2O_2), and light significantly impact the growth and metabolism of *F. graminearum*, which influence DON biosynthesis (13).

Past studies have demonstrated that *F. graminearum* can grow across a broad temperature range, with optimal DON production occurring at 22 °C–28 °C. Toxin biosynthesis can occur at 12 °C–37 °C, and the production ceases at temperatures > 37° (79). The optimal water activity (aw) for fungal growth ranges from 0.900–0.995, whereas DON biosynthesis requires a narrower range of 0.950–0.995 (80). This explains why FHB outbreaks and DON contamination are more prevalent in warm and humid regions, where the environmental conditions favor fungal proliferation and toxin production (81, 82).

Merhej et al. (83) investigated the effect of environmental pH on *F. graminearum* growth, DON biosynthesis, and *TRI* gene expression *in vitro* using liquid cultures on a minimal medium. Their results demonstrated that DON production and *TRI* expression were absent at neutral pH (84). However, by the third day of cultivation, the medium's pH dropped sharply, triggering the expression of *TRI5* and *TRI101* and initiating accumulation of DON. Further research revealed that the transcription factor PacC, a key component of the pH regulation system, plays a critical role in secondary metabolite biosynthesis. In a follow-up study, Merhej et al. (85) reported that the deletion of the *F. graminearum* PacC homolog (FgPAC1) led to earlier *TRI* gene induction and accelerated DON accumulation under acidic conditions, indicating that FgPAC1 could negatively regulate the *TRI* expression and DON biosynthesis (67).

Carbon and nitrogen sources, which are essential nutrients for microbial growth, also regulate DON biosynthesis in *F. graminearum*. Jiao et al. (86) analyzed the effects of 12 carbon sources on DON and 3-ADON production in nine 3-ADON-producing strains of *F. graminearum*. Sucrose, raffinose, and stachyose significantly enhanced trichothecene production across all tested strains. In sucrose-based media, the expression of *TRI4* and *TRI5* were significantly upregulated, whereas this effect was absent in glucose-based media (87). Furthermore, adding glucose to sucrose-based media did not inhibit DON accumulation, suggesting that trichothecene biosynthesis is not regulated by carbon catabolite repression (88). Instead, *F. graminearum* appears to directly recognize sucrose molecules, activating *TRI* expressions and initiating the trichothecene biosynthesis pathway (67).

In terms of nitrogen sources, guanidino-butyrate, arginine, and ornithine strongly induce DON biosynthesis, whereas ammonium, nitrate, leucine, and tyrosine exhibit inhibitory effects (89). The nitrogen metabolic regulator gene FgAREA is induced under

nitrogen-limiting conditions, which promotes secondary nitrogen utilization and activates the expression of *TRI*, including *TRI5*, *TRI6*, and *TRI10* (90). In contrast, FgNMR1, a co-repressor involved in nitrogen catabolite repression, inhibits FgAREA under nitrogen-sufficient conditions, thereby suppressing DON biosynthesis (91). However, the deletion of FgNMR1 alone does not significantly affect DON production (92).

Other chemical compounds can also influence DON biosynthesis. For example, H₂O₂ has been demonstrated to enhance DON and 15-ADON production by activating the *TRI* expression, particularly *TRI4*, *TRI5*, and *TRI12* (93). In contrast, adding catalase to cultures could significantly reduce *TRI* expression and DON accumulation. This regulatory effect is associated with oxidative stress-responsive transcription factors, including FgAP1, FgATF1, and FgSKN7. The deletion of FgSKN7 significantly reduced DON biosynthesis and impaired H₂O₂-induced *TRI* expression (94). Interestingly, the deletion of FgAP1 increased the DON production and enhanced the *TRI* expression, suggesting that the loss of FgAP1 disrupts oxidative stress regulation and triggers abnormal *TRI* overexpression (95).

In addition, ferulic acid has been exhibited to suppress *TRI* expression and reduce DON biosynthesis through transcriptional regulation (96). Boutigny et al. (97) demonstrated that DON production is inversely correlated with the initial ferulic acid concentration in the medium, with higher concentrations exerting stronger inhibitory effects.

4 Advances in the detoxification and control of DON

DON is chemically stable and highly resistant to heat, acidic conditions, and long-term storage, making its elimination difficult through the conventional processing methods. Therefore, the development of efficient, safe, and cost-effective detoxification strategies deemed is critical for ensuring food and feed safety. The current methods for mitigating DON contamination fall into three main categories: physical, chemical, and biological approaches.

The physical methods aim to remove or inactivate DON through techniques such as sorting, adsorption, irradiation, or thermal processing. Chemical methods involve the use of reagents, such as alkalis, ozone, or oxidants, to alter the molecular structure of DON and reduce its toxicity. Biological methods rely on microorganisms, enzymes, or plant metabolic pathways to adsorb, degrade, or transform DON. Among these, biological strategies are particularly promising owing to their mild operational conditions, high specificity, environmental sustainability, and ability to preserve the nutritional quality.

4.1 Physical methods

4.1.1 Thermal processing

Thermal treatment is the most commonly applied physical approach for reducing DON contamination. In general, higher temperatures yield better detoxification efficiency. The common techniques include steaming, baking, frying, canning, and extrusion (7). For instance, superheated steam treatment at 185 °C for 6 min reduced the DON levels in contaminated wheat by 52% (98, 99).

Frying at 169–243 °C decreased DON concentrations in wheat dough by 20–28%, whereas baking of bread led to 54% of 82% reduction (100). Despite these promising results, the mechanisms behind DON reduction during heating remain unclear. It remains unknown whether DON is fully degraded or simply adsorbed onto the food matrix. Moreover, the identity and toxicity of the resulting degradation products are not well characterized. Advantages—well-established technology with proven scalability; Limitations—the mechanisms of action and the toxicity of degradation products remain incompletely elucidated, and potential impacts on quality and nutritional attributes cannot be excluded.

4.1.2 Irradiation

Three primary irradiation techniques have been investigated in relation to DON degradation: gamma irradiation, electron beam irradiation, and ultraviolet (UV) irradiation. Khaneghah et al. (101) reported found that the efficiency of DON degradation by electron beam irradiation increased with higher doses, which was also influenced by the concentration of DON in the solution. Specifically, at doses of 1–10 kGy, higher solution concentrations resulted in greater degradation, whereas the detoxification rate of DON in the aqueous solution was 89.13% at 20 kGy (102). Irradiation exhibited greater effectiveness in aqueous environments, with little effect on DON in dry materials such as wheat and corn, limiting its applicability to solid commodities.

DON is also sensitive to UV light. Feizollahi et al. (103) demonstrated that UV irradiation significantly degraded DON, with enhanced efficacy detected under longer exposure times, shorter irradiation distances, and lower solution pHs. Shanakhat et al. (104) performed UV irradiation at 254 nm for 15, 30, 60, and 120 min on semolina to reduce the mycotoxin contamination. In fact, UV irradiation has been widely explored for degrading aflatoxins, albeit its application to DON remains limited. Moreover, the inconsistent performance, shallow penetration depth, and the potential to damage sensitive nutrients such as vitamins significantly constrain its practical utility in DON detoxification. Advantages—high degradation efficiency in aqueous systems; Limitations—poor penetration in solid matrices, narrow parameter windows, and unfavorable effects on sensitive nutrients.

4.1.3 Adsorption

A range of adsorbents is currently available in the market for DON removal, including activated carbon, inorganic aluminosilicates such as hydrated sodium calcium aluminosilicate (HSCAS), and organic materials such as glucomannan and yeast cell walls. Activated carbon can adsorb and remove 90.5% of DON and AFB1 (105). A newly developed composite adsorbent of HSCAS achieved an average DON adsorption rate of 90% (106). However, these adsorption method has several limitations. It often requires elevated temperatures or stringent conditions, and may non-selectively bind essential micronutrients in the food or feed. Furthermore, if DON is only adsorbed but not degraded, there is a risk of secondary contamination. Considering such concerns, the European Union does not permit the use of adsorbents for mycotoxin mitigation in animal feed. As such, adsorption is not considered the most reliable strategy for DON detoxification. Advantages—simple implementation and low cost; Limitations—lack of selectivity, concomitant adsorption of nutrients, risk of recontamination, and restricted regulatory acceptance.

4.2 Chemical methods

Chemical degradation methods involve the breakdown of functional groups on the DON molecule through exposure to strong acids, bases, or oxidants, with the aim of ultimately reducing or eliminating its toxicity. Common techniques employed for this include alkaline hydrolysis, ammoniation, and oxidation. DON is particularly sensitive to alkaline conditions and readily degrades in basic solutions. Treatment of DON-contaminated wheat with sodium carbonate (Na_2CO_3) and sodium bisulfite (NaHSO_3) yielded DON-reduction rates of 83.9 and 69.9%, respectively (7). These methods are most effective for high-moisture materials, such as silage and liquid fats, but less suitable for solid feeds such as oilseed cakes or bulk feed ingredients.

Ozone is a powerful oxidizing agent that can rapidly cleave double bonds in organic compounds. It exhibits excellent penetration ability and readily decomposes into oxygen without leaving any toxic residues. Moreover, ozone is easy to generate on-site, requires no storage or post-treatment, and has been widely recognized by researchers globally for its remarkable potential in practical applications. Among oxidants, ozone has received growing attention due to its strong oxidative potential. It targets the C9–C10 double bond in DON's structure, breaking it down into simpler, less toxic compounds such as acids, aldehydes, and ketones (107, 108). As illustrated in Figure 6, ozone reacts directly with the molecular structure of DON (109). In recent years, ozone has emerged as a widely studied and applied technique for controlling fungal growth and mycotoxin contamination in diverse food products. It effectively kills harmful microbes and insects, reduces pesticide residues, and extends the shelf life of stored grains.

Young et al. (108) demonstrated that ozone treatment effectively degraded DON in wheat and corn, with significantly better outcomes observed in humid ozone environments relative to that in dry ozone. Additionally, Yang et al. (110), based on their investigation of the degradation efficiency of ozonated water at different concentrations

on the trichothecene mycotoxins, proposed preliminary pathways for the formation of degradation products. Their findings consistently indicated that ozone was highly effective in degrading DON.

Obadi et al. (111) reported that ozone reacts with double bonds in carotenoid-like compounds, resulting in the reduction of the yellowness of flour and an increase in brightness. Ozone also reacts with the double bonds of unsaturated fatty acids, generating free radicals that can cause rancidity. In addition, ozone exposure was found to alter the gelatinization properties of starch. Bamyar et al. (112) further demonstrated that moderate ozone treatment enhanced the dough strength of wheat flour and reduced its extensibility; however, excessive ozone treatment led to a decrease in the ratio of unextractable polymeric protein to extractable polymeric protein (UPP/EP), indicating a potential degradation of the gluten quality.

Therefore, when applying ozone technology to degrade mycotoxins, it is essential to evaluate its impact on the nutritional value and the processing quality of grains. Presently, studies assessing the nutritional properties of major DON-contaminated commodities such as wheat and corn after ozone treatment remain limited. This lack of a comprehensive quality-evaluation system for ozone-treated raw materials directly restricts the broader application and commercialization of ozone detoxification technologies. Advantages—high efficiency with *in situ* generation, well-defined reactivity toward double bonds; Limitations—requires careful evaluation of impacts on dough rheology, lipid oxidation, color, and other quality parameters.

4.3 Biological methods

Despite the limited reports, recent studies both domestically and internationally, have demonstrated a significant progress in the biological degradation of DON. Microorganisms can secrete extracellular enzymes that catalyze various chemical reactions—such

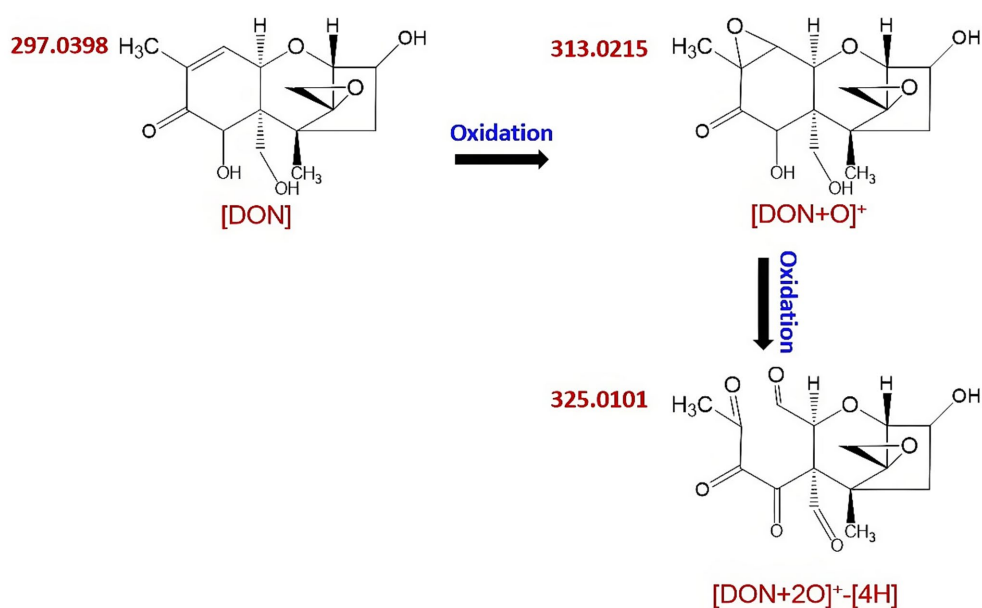


FIGURE 6
The chemical process of DON and ozone.

as de-epoxidation, deacetylation, hydroxylation, hydrolysis, and glycosylation—to convert DON into less toxic metabolites.

For example, Wang et al. (113) isolated a bacterial strain from soil that could use DON as its sole carbon source, which achieved a degradation efficiency of 63%. Liu et al. (114) screened and identified an effective DON-degrading *Bacillus* strain, which, when added to animal feed, reduced the DON levels by up to 50.69%.

Enzymatic degradation methods, particularly, offer high specificity and efficiency by exploiting the unique substrate affinity of enzymes to catalyze mycotoxin breakdown. These methods prevent toxin regeneration and are highly selective. Chen et al. (115) demonstrated that enzymes produced by *Gordonia hydrophobica* HAU421 could cleave the epoxide ring of trichothecenes, thereby significantly reducing the toxicity of DON.

Despite these advantages, the existing biological methods face several limitations. Their economic feasibility is low, and the inherent microbial activity fluctuates with the environmental conditions. The degradation process is typically slow, and it is challenging to apply these methods to solid matrices. Furthermore, the safety and composition of microbial metabolites are often difficult to evaluate. As a result, the presently known practical application of biological detoxification strategies for DON remains limited. Advantages—high specificity, mild conditions, and potential for selective biotransformation; Limitations—adaptation to solid matrices and industrial-scale application remain challenging, and the safety of metabolic products requires systematic evaluation.

5 Conclusion

This review consolidates mechanistic insights into DON biosynthesis and its regulation, emphasizing the TRI cluster, transcriptional control, signaling cross-talk, and environmental modulation. While pathway enzymes and key regulators are increasingly well mapped, context-dependent TRI expression and matrix-specific detoxification efficacy remain major sources of variability.

Currently, chemical fungicides are widely being used to manage FHB during agricultural production. However, concerns regarding chemical residues and environmental contamination underscore the urgent need for eco-friendly control strategies. A deeper understanding of the biosynthetic and regulatory mechanisms governing DON production in *F. graminearum* provides a crucial foundation for developing more sustainable disease management approaches.

Each detoxification strategy presents unique strengths and limitations. The known physical methods are scalable but may leave toxic residues. Chemical approaches are effective but can damage product quality or pose safety risks. Biological methods offer specificity and sustainability but are constrained by process complexity and scalability. Therefore, the choice of detoxification method should consider not only efficacy but also safety, regulatory compliance, and compatibility with food/feed matrices.

6 Prospects

Future research should focus on leveraging gene editing technologies to enhance the endogenous resistance to DON and breeding new wheat cultivars with both FHB resistance and reduced

toxin accumulation. In parallel, the hybrid methods, such as combining physical, chemical, and biological techniques, to maximize the detoxification efficiency. Innovations in enzyme engineering and microbial synthetic biology may yield more robust strains and catalytic tools. Moreover, regulatory frameworks must evolve to evaluate detoxification products comprehensively and guide the safe implementation of biological methods in the food industry.

These advancements of advancements in gene editing, enzyme engineering, and hybrid detoxification methods could offer promising solutions for mitigating FHB outbreaks and ensuring global food security.

Author contributions

MH: Investigation, Writing – original draft. YL: Writing – original draft, Formal analysis, Validation. HY: Formal analysis, Validation, Writing – original draft. XG: Funding acquisition, Writing – review & editing. CS: Funding acquisition, Writing – review & editing, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft.

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Conflict of interest

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