Received: 3 August 2019 | Revised: 24 December 2019 | Accepted: 20 January 2020

DOI: 10.1111/1541-4337.12545

COMPREHENSIVE REVIEWS IN FOOD SCIENCE AND FOOD SAFETY

Comprehensive REVIEWS in Food Science and Food Safety WILEY

Deoxynivalenol: Masked forms, fate during food processing, and potential biological remedies

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Funding information
Synergistic Innovation Center of Food Safety and Nutrition; National First-class Discipline Program of Food Science and Technology, Grant/Award Number: JUFSTR 20180303; National Natural Science Foundation of China, Grant/Award Number: 31772069

Abstract

Deoxynivalenol (DON) has drawn global attention because of its prevalence and significant effects on human or animal health. Biological remedies for DON have been developed from preharvest to postharvest. Applying microbes, including bacteria, fungi (yeast and molds), and enzymes, results in inhibited synthesis, structural destruction, or adsorption of DON. DON can be degraded into masked forms by phase I metabolism or phase II metabolism. During food processing, DON content changes dynamically and is even transformed. Physical, chemical, thermal, or biological processes physically reduce DON content. Temperature, heating time, enzymes, food additives, microorganisms, food composition, contamination level, and other ingredients are key factors. Although DON content can be reduced during food processing, increases in other toxins, such as DON-3-β-D-glucoside and 3-acetyl-DON, can be potentially risky. The application of biodegradation methods in food processing bears research significance. Both microorganisms and enzymes can be potentially used. Novel techniques, such as RNA interference, omics technologies, or enzymes coupled with the genetic engineering method, can be introduced. This review systematically updates the understanding of masked forms of DON, biological degradation strategy, fate of DON during processing, and future trends for biodegradation. Challenges to the successful application of biological methods may include the stability and suitability of the detoxification agents, security of degradation products, and successful application for industrial production.

KEYWORDS

biological degradation, deoxynivalenol, food processing, masked forms, RNA interference

1 | INTRODUCTION

Contamination with trichothecene mycotoxins and their derivatives is a global issue in food safety, with deoxynivalenol (DON) being the most prevalent. DON is commonly found in wheat, corn, barley, rye, oat, and safflower seed, among others (Bennett & Klich, 2003). DON contamination is prevalent in Africa, Asia (particularly in China), America, Europe, and the Middle East. A survey of 17,316 samples worldwide from 2004 to 2011 showed that compared with zearalenone (ZEN), aflatoxins (AF), fumonisins (FB), and ochratoxin A (OTA), DON was the most dominant, with an incidence of 55% (Streit, Naehrer, Rodrigues, & Schatzmayr, 2013). Another survey was conducted in 2018, and this included 13,629 samples from 77 countries worldwide and suggested that DON is one of the widespread toxins, with contamination rates in various continents determined as follows: Asia, 80%; Europe, 63%; Africa, 75%; South and Central America, 67%; North America, 67%; and the Middle East, 65% (Biomin, 2019). DON attracts global attention because of its prevalence and significant effects on human or animal health. Therefore, control strategies need to be

developed to prevent, eliminate, or inactivate DON in foods and feeds.

DON contamination can be a dynamic process occurring from preharvest to processing (Pitt, Taniwaki, & Cole, 2013). Control strategies for DON from farmland to foods and feeds have been developed to (a) inhibit the production or contamination of DON before harvest; (b) degrade or remove DON from contaminated food and feed; (c) reduce the bioavailability of DON by reducing gastrointestinal absorption. The spread of mycotoxins in the field can at times be difficult to control (Awad, Ghareeb, Böhm, & Zentek, 2010). Methods of DON decontamination can be divided into chemical, physical, and biological approaches. Considerable success has been achieved in the control of DON; however, these methods have certain limitations. The processes involved in the physical and chemical methods are difficult to control, require additional instruments, or entail higher costs. For chemical methods, potentially harmful substances may remain. With the aforementioned disadvantages considered, biodetoxification has emerged as a potential technique. Microbial methods are specific, efficient, and environmentally safe; in addition, the conditions required to accomplish these techniques are mild and induce reduced effects on the quality and palatability of foods or feeds. Enzymes produced by organisms can also be potential degradation agents. Use of selected microorganisms was considered as the best strategy to decontaminate mycotoxins. They are the main organisms suitable for mycotoxin mitigation (Awad et al., 2010). The use of whole bacterial cells in industrial applications may be the most feasible means of remission (Bullerman, Giesova, Hassan, Deibert, & Ryu, 2006; Hassan & Bullerman, 2013). Some microorganisms and enzymes have been applied for patent and regarded as potential feed additives (Gao et al., 2018).

Moreover, DON is highly susceptible to transformation. Several masked forms of DON have been reported. Regardless, the established standards and detection methods for modified forms of mycotoxins remain inadequate. The formation and mutual transformation of these modified toxins may lead to underreporting of mycotoxin levels, particularly for DON-3-β-D-glucoside (D3G) (Freire & Sant'Ana, 2018). The toxicity and metabolic mechanisms of these modified forms need to be determined and investigated (Berthiller et al., 2013; Brodehl, Möller, Kunte, Koch, & Maul, 2014). These questions should be seriously considered in the study of DON detoxification.

This review discusses the fate of DON during food processing such as bread making. We present an update of studies conducted on the microbial degradation of DON, including bacteria (lactic acid bacteria, bacteria from soil, bacteria from plant, rumen and intestinal bacteria), yeast, and enzymes. We also show the toxicity of masked forms of DON and future trends in studying the degradation of DON (Figure 1).

2 | TOXICITY OF DON AND ITS MODIFIED FORMS

DON is categorized as a type B trichothecene and is the most common form of trichothecene. Classified under Group 3 by the International Agency for Research on Cancer, DON is noncarcinogenic. DON may induce acute toxicity, gastrointestinal toxicity, hepatotoxicity, immunotoxicity, developmental toxicity, reproductive toxicity, neurovirulence, ribosomal toxicity, and so on. Research into the mechanism of action of DON suggests that the toxic effects of DON are related to oxidative stress, mitochondrial apoptosis, endoplasmic reticulum stress (ER), ribosome stress, lipid peroxidation, and the mitogen-activated protein kinase (MAPK) signal pathway (Dinu et al., 2011; Zhang, Jiang, Geng, Cao, & Zhong, 2009). In animals and humans, DON induces anorectic, reduced food intake, and vomiting effects, and those responses are regulated by central and peripheral nervous systems. Hypothalamus and brainstem play pivotal roles of both long- and short-term regulation in food intake (Hussain & Bloom, 2013). Besides, reduced nutrient absorption and reduced food intake are related with intestinal factors, such as hormone, and pro-inflammatory cytokines (Terciolo, Maresca, Pinton, & Oswald, 2018).

The term "modified mycotoxins" refers to all forms derived from mycotoxins. DON is highly susceptible to transformation because of plant responses, detoxification, matrix effects, metabolism, and food processing, among others (Freire & Sant'Ana, 2018). Most studies focus on the cytotoxicity, intestinal toxicity, and immunotoxicity of modified forms, whereas neurotoxicity, nephrotoxicity, and reproductive are rarely discussed (Figure 1). Data on 3-keto-4-deoxynivalenol (3-keto-DON) remain lacking. The number and position of epoxy, hydroxyl groups, and ester groups influence the toxicity of trichothecenes (Nagy, Fejer, Berek, Molnar, & Viskolcz, 2005). Thus, most modified forms of DON are less toxic than free DON.

Modified forms of DON, as well as their metabolism and transformation in vitro or in vivo, are shown in some reports (Figure 2). Among them, the acetylated and glycosylation forms are the most important and have been mostly studied. Before being absorbed by animals or humans, a considerable part of DON and masked forms can be transformed by microorganism. Liver is the main phase II transformation site, and the hydrophilic substances produced are mainly excreted in urine (Figure 2a). Animal models, human models, mammalian cell models, plant models, and microbial organism models have been used in toxicity or metabolic studies for derivatives. Regardless, discrepancies in the investigation of their toxicity and metabolism are noted, particularly the detoxification products. Some modified forms of DON can be converted to free forms during digestion, potentially increasing the risk for humans and animals. The aforementioned cases

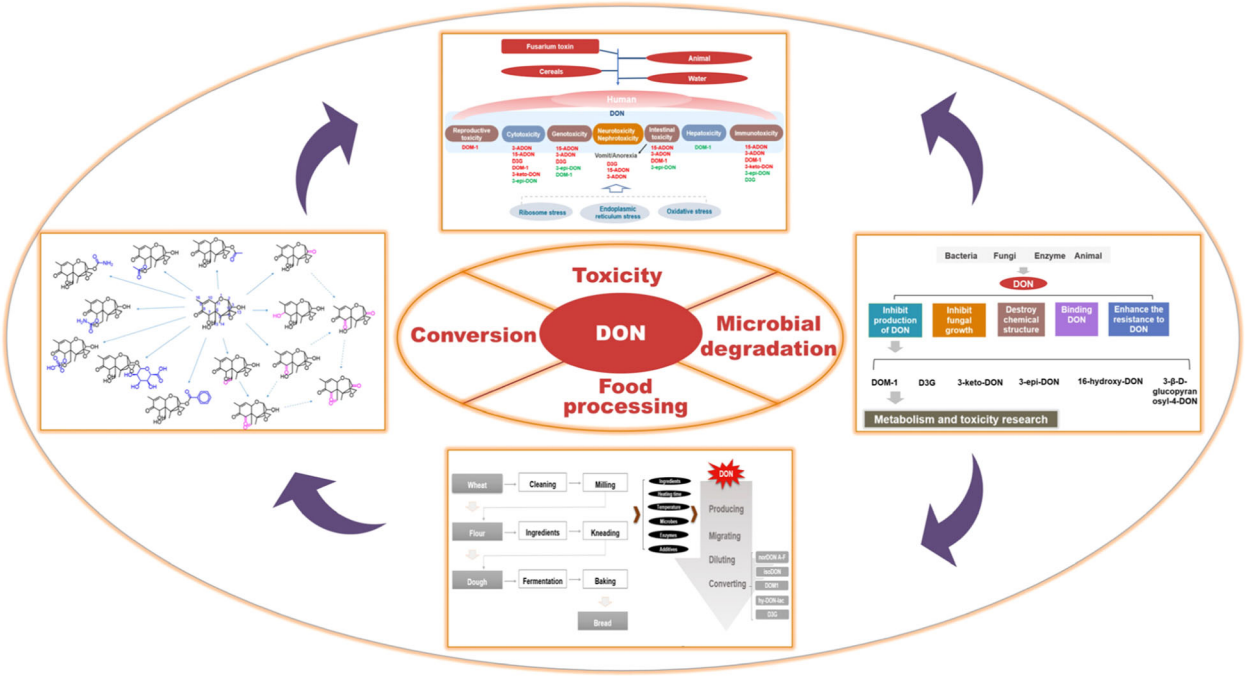

FIGURE 1 Framework of the review. In the summary of toxicity of DON and modified forms, red indicates toxicity and green represents nontoxicity or negligible toxicity

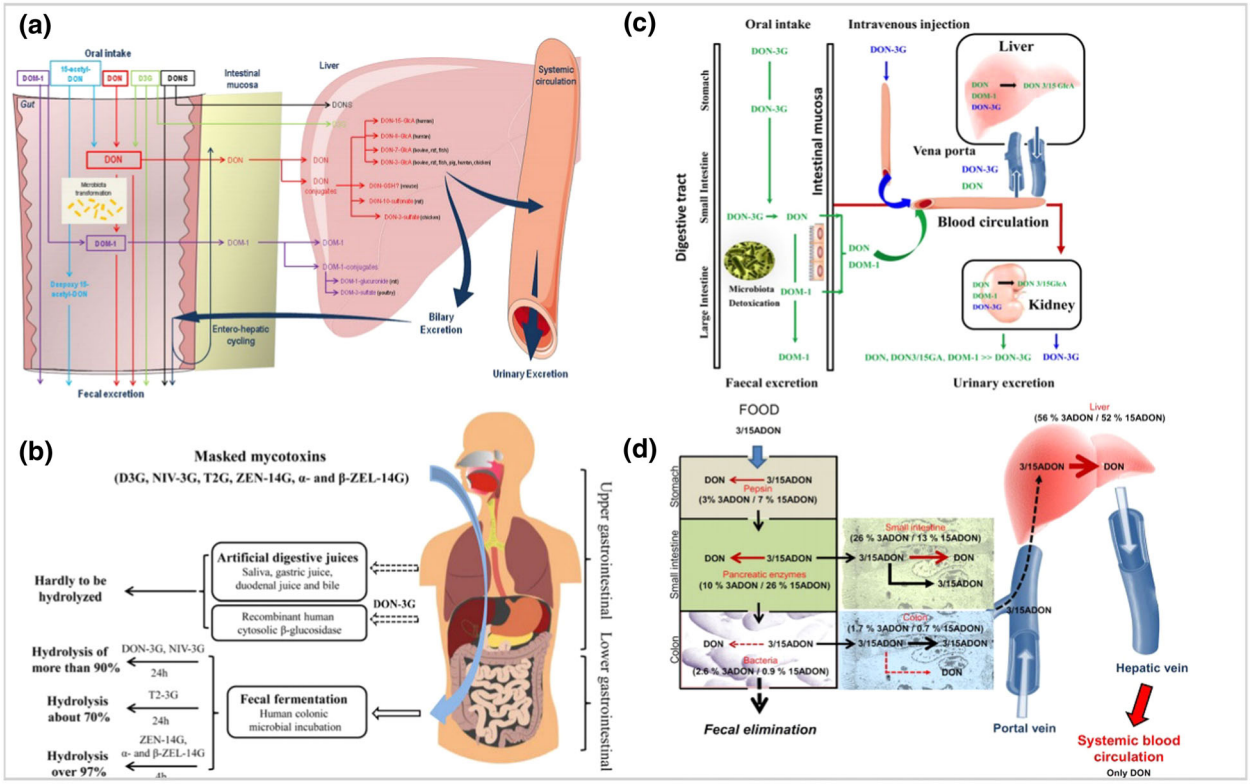

FIGURE 2 Metabolism of DON and its modified forms in vivo and in vitro. (a) Metabolism of DON and its modified forms in humans and animals (Payros et al., 2016). (b) Metabolism of masked mycotoxins according to in vitro reports (Zhang et al., 2019). (c) Metabolism of D3G in pigs (Zhang et al., 2019). (d) Deacetylation of 3-ADON and 15-ADON in humans (Ajandouz et al., 2016)

may result in more serious hazards than those estimated based on the initial toxin level only (Khaneghah, Martins, von Hertwig, Bertoldo, & Sant'Ana, 2018).

Published modified forms of DON include (a) acetylated forms (for example, 3-acetyl-DON [3-ADON] and 15-acetyl-DON [15-ADON]); (b) epimer forms (for example, 3-epi-deoxynivalenol [3-epi-DON]); (c) glycosylation forms (for example, D3G); (d) hydration forms; (e) oxidation forms (for example, 3-keto-DON and deepoxy-DON [DOM-1]); (f) sulfate forms (for example, DON sulfonate [DONS]); (g) processing products (for example, norDON A, norDON B, norDON C, and norDON F); and (h) other modified forms, (for example, DON-3-diglucoside, DON-3-triglucoside, and DON-3-tetraglucoside).

If biochemistry refers to the conversion of chemically similar compounds by catalytic enzymes, associating all compounds directly by their chemical similarity may be logical. The canonical SMILES deposited in or computed by PubChem for DON is *CC1 = CC2C(C(C1 = O)O)(C3(CC(C(C34CO4)O2)O)C)CO*, which could be regarded as the seed for generating similar molecular structures. Substructure fingerprints within the PubChem database (Tanimoto chemical similarity >700) were used to perform similarity-based modified DON (Table S1). When the Tanimoto chemical similarity was 1,000, these modified DONs were classified into six main groups (Figure 3). In Figure 3a, DON and DON isomers change in molecular structures. These compounds are mainly DON isomers, which have the same molecular weight as that of DON ($C_{15}H_{20}O_6$); some bones may isomeric changed, similar to alpha-to-beta molecular configuration. Figures 3b, 3d, and 3e show acetyl-modified DONs; Figure 3f presents di-acetyl modified DONs; and Figure 5c shows DONs modified by oxidation–reduction. Other modified DONs, such as D3G, DONS, and DOM-1, were regarded as tiny groups consisting of less than four compounds.

2.1 | 3-ADON and 15-ADON

3-ADON and 15-ADON are acetylated forms of DON produced by *Fusarium culmorum* and *Fusarium graminearum*, which frequently occur in food and feed. The metabolism of acetylated forms largely varies because of the differences in the evaluation model. DOM-1, DON-GlcA, and DON are metabolites in animal models. A special interest is the transformation of acetylated forms into free DON in vivo.

Acetylated forms can be absorbed more rapidly than DON in animal models for oral intake assay (Broekaert, Devreese, De Baere, De Backer, & Croubels, 2015). In an in vivo experiment in chicken, 3-ADON was transformed to DOM-1 and free DON, and 15-ADON was metabolized to DOM-1, free DON, and deepoxy-15-acetyl-DON (Young, Zhou, Yu, Zhu, & Gong, 2007). Regardless, metabolites of acetylated forms in pigs were DOM-1, DON, DON glucuronide (DON-GlcA), and trace acetylated forms. Oral bioavailability of acetylated forms in pigs was higher than that in chickens (Broekaert, Devreese, De Mil, et al., 2015; Eriksen, Pettersson, & Lindberg, 2003; Maresca, 2013). In calves, 3-ADON and 15-ADON were rapidly converted into free DON. DON-3-GlcA was the major metabolite of DON and acetylated forms. Scarce DON-15-GlcA was found in urine (Valgaeren et al., 2019). Another study conducted both in vivo (in human liver, small intestine, and kidney) and in vitro (in HepG2 cells, Caco-2 cells, and T84 cells) confirmed complete deacetylation fate of 3-ADON and 15-ADON, and liver and small intestine were identified as the main site of deacetylation reaction in humans (Figure 2d). Digestive enzymes, bacteria, intestinal, liver, and colon participated in the deacetylation process, and only free DON was found in the systemic blood. Once consumed, 3% and 7%, 10% and 26%, 2.6% and 0.9%, 26% and 13%, 1.7% and 0.7%, and 56% and 52% of 3-ADON and 15-ADON were deacetylated by pepsin, pancreatic enzymes, colonic bacteria, small intestine, colon, and liver, respectively, resulting in no acetylation forms in the whole blood circulation (Ajandouz et al., 2016).

MAPK is an important transmitter of signals from the cell surface to the nucleus. It is one of the well-known signal transduction pathways of cell proliferation, stress, inflammation, differentiation, and apoptosis. ERK, ERK5, p38, and JNK are subgroups of MAPK. Similar to DON, 15-ADON and 3-ADON were able to activate the ERK/MAPK, p38/MAPK, and JNK/MAPK pathways in vitro and in vivo. In addition, 15-ADON exerted the same ability at a lower dose than those to 3-ADON or DON (Pinton et al., 2012). However, only two hydrogen bonds were formed. Figure 4 shows the MAPK pathway analysis of DON and modified DON.

The comparative toxicity of these two toxins exhibited no agreement. Some cytotoxic assays indicated that 3-ADON was more toxic than 15-ADON (Juan-García, Juan, Tolosa, & Ruiz, 2019; Juan-García, Taroncher, Font, & Ruiz, 2018); however, other studies found 15-ADON to be more toxic (Pinton et al., 2012). The intestinal toxicity, immunotoxicity, oxidative stress, genotoxicity, and cytotoxicity of acetylated forms have been studied in vitro or in vivo (Table 1).

2.2 | DON-3-β-D-glucoside

D3G is the phase II metabolite of DON by glycosylation. D3G remains stable in the human upper gut. It is resistant to acidic pH, cytosolic-β-glucosidase, and digestive pancreatic enzymes. Commonly, D3G is less toxic than DON. In cereals and cereal by-products, the contamination level of D3G reached half that of DON. The ratio of D3G/DON reached 20% in grains and even exceeded 100% after processing (Berthiller et al., 2009; Berthiller et al., 2013; Varga, Malachova, Schwartz, Krska, & Berthiller, 2013).

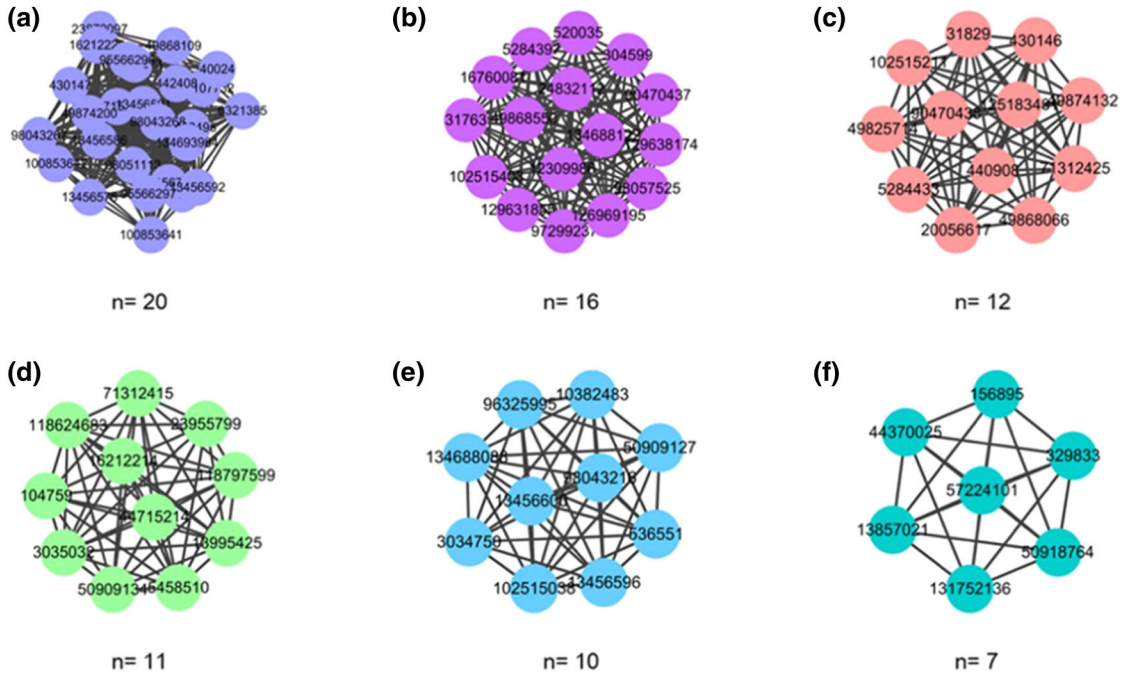

FIGURE 3 Tanimoto chemical similarity-based modified DON network, classified into six main groups; the number of modified DONs is noted. The similarity score is 1,000. (a) DON and DON isomeric change molecular structures. (b), (d), and (e) Acetyl-modified DONs. (c) Oxidation/reduction-modified DONs. (f) Di-acetyl modified DONs

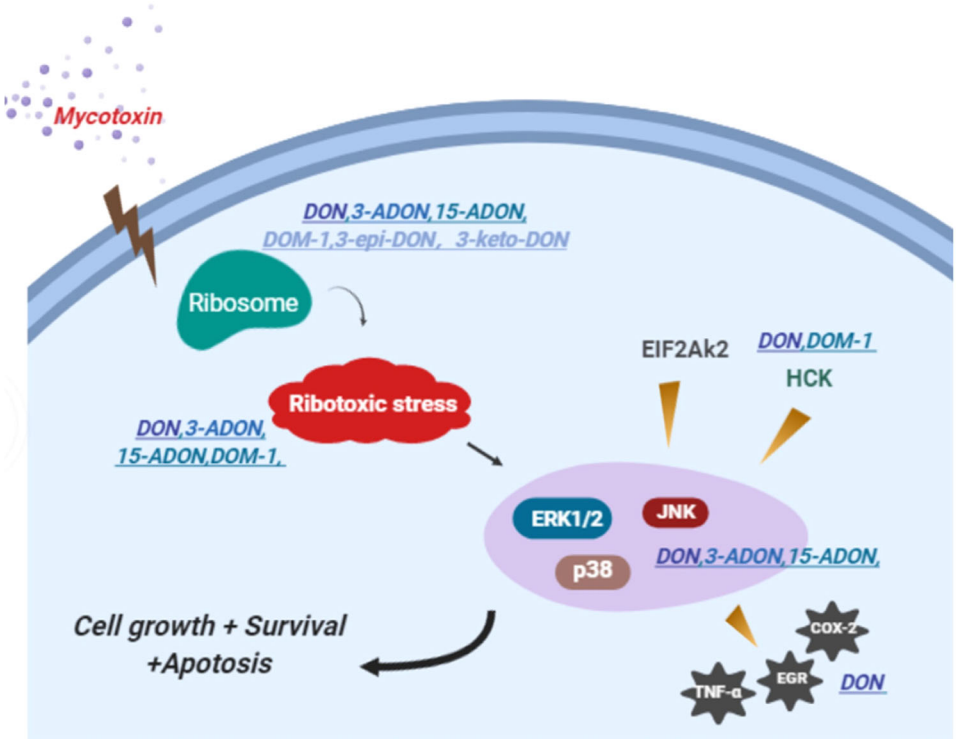

FIGURE 4 Ribotoxic stress and MAPK pathway analysis for DON and modified DON

(a) DON, 3-ADON, 15-ADON, DOM-1, 3-keto-DON, and 3-epi-DON bind to the A-site of the peptidyl transferase center of the ribosome, whereas D3G loses its binding ability. (b) Some studies indicate that only DON, 3-ADON, 15-ADON, and DOM-1 exert ribotoxic stress, and 3-ADON, 15-ADON, 3-keto-DON, and 3-epi-DON form only two hydrogen bonds. (c) DON, 3-ADON, 15-ADON, and DOM-1 can evoke the $ERK_{1/2}$, JNK, and p38 MAPK pathways. Moreover, DON and DOM-1 can activate the upstream channel of MAPK, such as HCK and EIF2AK2. DON activates the downstream channels of MAPK, such as EGR, COX, and TNF-α. For DOM-1, there is no agreement on the above information. Because DOM-1 cannot evoke MAPK pathway in IPEC-J2 cells, Caco-2 cells, or jejunal explants

TABLE 1 Toxicity of 3-ADON and 15-ADON *in vitro* and *in vivo*. (Adapted from Broekaert *et al.* (2015a))

Mycotoxin	Model	Douse	Exposure time	Effect	IC_{50}	Reference
15-ADON	HepG2	0 to 1.5 μM	0–120 min	Increase ROS	8.1 μM (24h)	(Juan-García *et al.*, 2019)
		0.2 to 1.5 μM	48/72h	Lipid peroxidation	5.3 μM (48 h)	
					5.2 μM (72h)	
15-ADON	HepG2	0.5 to 1.5 μM	48 h	Increase G0/G1, decrease S and G2/M	6 μM (24h)	(Juan-García *et al.*, 2018)
					1.9 μM (48h)	
		3 μM	48 h	Decrease G0/G1 and S, increase G2/M	2.0 μM (72h)	
15-ADON	IPEC-1	0 to 30 μM	24 h	69% inhibition cell proliferation	\	(Pinton *et al.*, 2012)
		10 μM	48 h	75% reduction of transepithelial electrical resistance		
15-ADON	IPEC-1	0 to 150 μM	24 h	EC_{80} of 10.7 μM	\	(Alassane-Kpembi, Puel, & Oswald, 2015)
15-ADON	Caco-2	0 to 30 μM	6 h	No significant effect on cell viability	\	(Kadota *et al.*, 2013)
		3 μM	6 h	Damage to tight junctions in luciferase yellow assay		
		0 to 3 μM	72 h	Significant dose-dependent increase of IL-8		
15-ADON	MIN-GL1/K562	\	\	CD_{50} 6/1.2 μM	\	(Visconti, Minervini, Lucivero, & Gambatesa, 1991)
15-ADON	3T3	0.5 to 14.8 μM	24 h	50% DNA synthesis inhibition at 1.51 μM	1.51 mM	(Eriksen, Pettersson, & Lundh, 2004)
15-ADON	Mice	2.5 mg/kg bw PO	2/6 h	Altered cytokine expression	\	(Wu et al., 2014a)
15-ADON	piglets	1240 μg DON, 935 μg 15-ADON	4 weeks	Decreased villus height compared to solely DON equivalent	\	(Pinton *et al.*, 2012)
3-ADON	IPEC-1	0 to 30 μM	24 h	13% inhibition of cell proliferation	\	(Pinton *et al.*, 2012)
		30 μM	48 h	Transepithelial electrical resistance unaffected		
3-ADON	IPEC-1	0 to 150 μM	24 h	EC_{80} of 126 μM	\	(Alassane-Kpembi et al., 2015)
3-ADON	Caco-2	0 to 0 μM	6 h	No significant effect on cell viability	\	(Kadota et al., 2013)
		0 to 3 μM	72 h	Significant dose-dependent increase in IL-8		
3-ADON	MIN-GL1/K-562	\	\	CD_{50} 21\6 μM	\	(Visconti *et al.*, 1991)
3-ADON	3T3	0.9 to 29.6 μM	24 h	50 % DNA synthesis inhibition at 14.4 μM	14.4 mM	(Eriksen et al., 2004)
3-ADON	Mice	34 mg/kg bw PO, 49 mg/kg bw IO	Blous	LD50	\	(Ueno, 1984)
3-ADON	Mice	2.5 mg/kg bw PO	2/6 h	Altered cytokines expression	\	(Wu et al., 2014a)
3-ADON	HepG2	0.2 to 1.5 μM	48/72 h	Lipid peroxidation	6.2 μM (24h)	(Juan-García *et al.*, 2019)
					3.6 μM (48h)	
					5.2 μM (72h)	
3-ADON	HepG2	1.5 μM	48 h	Decrease G0/G1, S, G2/M	3.9 μM (24h)	(Juan-García *et al.*, 2018)
		3 μM	48 h	Decrease G0/G1, S, and G2/M	1.46 μM (48h)	
		0.5 μM	48 h	Micronuclei induction increase G0/G1, decrease S and G2/M	1.9 μM(72h)	

The transformation of masked forms of DON into free DON revealed the risk of colonic epithelium for exposure to free DON. Metabolism of D3G was conducted both in vitro and in vivo. DON, DON-GlcA, and DOM-1 were detected in the analysis. In vitro, D3G was hardly hydrolyzed by the upper digestive tract and other human digestive fluids, but can be hydrolyzed by the lower digestive tract (Figure 2b). In vivo, oral administration, PO administration, and intravenous administration experiments demonstrated that almost all D3G was hydrolyzed in the gastrointestinal tract of pigs (Figure 2c). D3G can be partly metabolized into free DON after incubation with human microbiota in vitro for 8 hr, such as *Enterococcus faecium* and *Lactobacillus plantarum* (Berthiller et al., 2011). Another in vitro study for mixed human fecal microbiota obtained similar results; the conversion efficiency reached 100% (Gratz, Duncan, & Richardson, 2013).

The metabolism of D3G in vivo has been elucidated by oral intake and intravenous injection with animals or humans. A recent study involving humans demonstrated that D3G was 84% absorbed by volunteers. Most D3G was absorbed as DON. DON-3-GlcA and DON-15-GlcA were the main metabolites (Mengelers et al., 2019). According to metabolic analysis of pigs for 24 hr, D3G was mostly excreted into DON, DOM-1, DON-15-GlcA, and DON-3-GlcA after the pigs were fed with D3G. Trace metabolites were found in the feces. D3G was administered intravenously and was almost completely hydrolyzed in the intestinal tract (Nagl et al., 2014). A study on rats concluded that D3G liberated DON as an intermediate metabolite in the digestive tract, but DON was poorly absorbed (Nagl et al., 2012).

2.2.1 | In vitro toxicity

Both the phytotoxicity and cytotoxicity of D3G were revealed in in vitro experiments. D3G was considerably less toxic than DON. Data on D3G were scarcely reported.

In the plant germ extract with an in vitro transcription and translation system, luciferase activity was slightly inhibited by D3G but significantly inhibited by DON (Poppenberger et al., 2003). D3G could not bind to the A-site of the ribosome peptidyl transferase center, indicating the absence of ribosome stress in D3G. In Caco-2 cells, the JNK/MAPK pathway and the p38/MAPK pathway could not be activated by D3G. No influence on viability and barrier function was observed (Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Liaubet, et al., 2016). D3G showed no toxicity in GSE-1 cells (Yang, Yu, Tan, Liu, & Wu, 2017). By contrast, cell viability in IPEC-J2 cells was influenced by D3G but was independent of D3G concentration. The cytotoxicity of D3G was far less than those of 3-ADON, DON, and 15-ADON (Broekaert et al., 2016).

2.2.2 | In vivo toxicity

Animal, intestinal explants, and microbial organism have been introduced in toxicity studies of D3G. Similar to DON, D3G caused anorexia in animals but induced extremely limited toxicity for other toxicity parameters.

In porcine jejunal explants, D3G exerted no effect on morphological lesions, histomorphology, and pro-inflammatory cytokines, including IL-1α, IL-1β, TNFα, IL-8, IL-22, and IL-17A (Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Liaubet, et al., 2016). A study involving mice also concluded that pro-inflammatory biomarkers such as splenic cytokine and chemokine mRNA could not be evoked by D3G. In the mouse model of nocturnal food consumption, D3G induced anorexia for up to 6 hr. The minimum nocturnal doses for D3G and DON were 5 and 0.05 mg/kg body weight (bw) (Wu, He, et al., 2014; Wu, Zhou, et al., 2014). A study on a *Saccharomyces cerevisiae PDR5* mutant strain demonstrated the extremely low toxicity of D3G; no change in growth rate was observed, and differences in DNA microarray analysis were small, with only 10 genes extracted.

2.3 | Deepoxy-DON

DON can be biologically transformed into DOM-1 by intestinal microorganisms. In chickens and turkeys, DOM-1 was metabolized as DOM-3-sulfate by oral ingestion (Schwartz-Zimmermann et al., 2015). DOM-1 did not activate the phosphorylation of the MAPK pathway in IPEC-J2 cells, Caco-2 cells, or jejunal explants, such as p38/MAPK, JNK/MAPK and $ERK_{1/2}$/MAPK, and Sapk/JNK (Pierron, 2016; Springler et al., 2017). DOM-1 retained the ability to fit into the A-site of the ribosome peptidyl transferase, and only two hydrogen bonds were formed. Thus DOM-1 lost the ability to activate ribosomal stress (Pierron, 2016).

2.3.1 | In vitro toxicity

Most in vitro studies have demonstrated that DOM-1 does not promote apoptosis or necrosis. These findings indicate that the opening of the 12,12-epoxy ring of DON leads to the absence of apoptotic toxicity.

DOM-1 showed no significant effects on the viability of RAW 264.7 cells, Jurkat T cells, RTgill-W1, IPEC-1, Caco-2 cells, and IPEC-J2. In addition, DOM-1 hardly influenced membrane integrity, barrier function, cellular metabolism, intracellular ATP, caspase-3, GSH/GSSG ratio, reactive oxygen species (Springler et al., 2017), mitochondrial activity, cytochrome c, and Bcl-2 (Nasri, Bosch, Ten Voorde, & Fink-Gremmels, 2006). The IC_{50} of DOM-1 was 55 times higher than that of DON in 3T3 fibroblasts (Eriksen, Pettersson, & Lundh, 2004). In study of bovine peripheral blood mononuclear cells, no IC_{50} was determined because the maximum inhibition was 24% (Daenicke, Keese, Goyarts, & Döll, 2011). Meanwhile, in HepG2 cells, DOM-1 reduced albumin release at rather high concentrations (Mayer et al., 2017).

Considering the presence of DOM-1 in ovarian follicular fluid, the effects of DOM-1 on the reproductive system of

cattle have also been evaluated. Notably, DOM-1 increased the apoptosis of bovine ovarian theca cells (1 ng/mL) and reduced the secretion of testosterone and progesterone (0.5 ng/mL). Moreover, the mRNA abundance of proteins related to ER stress was increased. The EIF2AK2, $ERK_{1/2}$, HCK, and AKT pathways were activated by DOM-1 (Guerrero-Netro, Estienne, Chorfi, & Price, 2017). ER stress may be one of the toxic mechanisms of DOM-1 in theca cells. These findings contradicted previous research.

2.3.2 | In vivo toxicity

Generally, DOM-1 retained the immune modulatory effects of DON but exerted no response on hepatotoxicity and proinflammatory cytokines. Studies were conducted using pure DOM-1 or DON with degradation substance.

Only three published articles have thus far been found on the toxicity of pure DOM-1 in vivo. In this study, BBSHN 797 was used to biotransform purified DON into DOM-1. DOM-1 was then purified by solid-phase extraction. Pigs administered with low and high levels of DOM-1 (0.14 or 0.3 mg/kg bw per day) weighed more, compared with the control and DON groups (0.15 or 0.3 mg/kg bw per day) at Week 2. No significant effects were observed on intestinal morphology, liver, mRNA expression of IL-6, IL8, IL-10, IL-1β, IL-1α, IL-17A, IFN-γ, TNF-α, TGF-β, and CCL20 in the DOM-1 groups. With regard to immunity parameters, spleen histology was significantly affected, whereas mesenteric lymph nodes were moderately affected (Pierron, 2016). In intestinal explants, DOM-1 caused no intestinal lesions and did not affect the expression of inflammatory cytokines. Genomic transcriptomic profiling revealed no differentially expressed genes on intestinal explants treated with DOM-1 (Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016). With regard to histopathology, the PCNA level, and antibody response, DOM-1 induced similar immune effects on DON in the pig model. Minimal intestinal toxicity and no hepatotoxicity were observed (Pierron et al., 2018).

Other studies on DOM-1 were conducted by adding bacteria or substances with degrading functions to DON. Studies on swine and pig exposure to DON detoxified with bacterial or enzyme demonstrated the elimination toxicity of DOM-1, considering that no influence on food intake or weight was observed (Grenier et al., 2013; Li et al., 2011).

2.4 | 3-epi-DON

3-epi-DON is the epimer of DON. The detoxification strategy that isomerizes the C3-OH of DON leads to the formation of 3-epi-DON. 3-epi-DON can be obtained by degrading DON with bacteria from soil.

Published data on the toxicity or metabolism of 3-epi-DON are lacking. The destruction of the C3-OH group in DON almost eliminates toxicity.

2.4.1 | In vitro toxicity

Similar to DOM-1, 3-epi-DON did not affect oxygen consumption, barrier function, cell viability, and intestinal lesions in Caco-2 cells (Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016). Owing to the selection of the analytical methods, the results changed substantially. The IC_{50} of epi-DON was 357 and 1,181 times higher than that of DON in Caco2 cells and in 3T3 mouse fibroblasts, respectively, as determined by MTT assay and BrdU assay (He et al., 2015).

2.4.2 | In vivo toxicity

On the basis of animal experiment results, 3-epi DON was nearly nontoxic. The bonding between 3-epi-DON and the A-site of the ribosome peptidyl transferase center resulted in only two hydrogen bonds. Consequently, the p38/MAPK and JNK/MAPK pathways cannot be activated by 3-epi-DON (Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016).

Intestinal explants treated with 3-epi-DON induced no differential expression of genes and no inflammatory response (Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016). In mice, oral exposure to 3-epi-DON for 14 days (25 and 100 mg/kg bw per day) induced no change in body weight, organ weight, organ histopathology, and hematology (He et al., 2015).

2.5 | 3-keto-DON

3-keto-DON is produced in the two-step enzymatic epimerization of DON. It may be converted into 3-epi-DON by bacteria such as *Devosia mutans* 17-2-E-8 (Hassan et al., 2017). Recent studies have determined that 3-ADON and 15-ADON can be degraded as 3-keto-DON by bacteria, with DON as an intermediate (Wang et al., 2019).

2.5.1 | In vitro toxicity

Several studies have investigated the toxicity of 3-keto-DON. The IC_{50} values of 3-keto-DON in Caco-2 and NIH/3T3 cells were 3.03 and 4.54 times higher than those of DON, respectively, as determined by MTT and BrdU assays (He et al., 2015). The immunotoxicity of 3-keto-DON was markedly reduced by 90% in mouse spleen lymphocytes owing to the oxidization of C3-OH into keto in DON (Shima et al., 1997).

2.5.2 | In vivo toxicity

No studies on the in vivo toxicity of 3-keto-DON have thus far been published.

3 | FATE OF DON DURING FOOD PROCESSING

Wheat is the most widely planted and most traded crop worldwide. Wheat is also one of the main crops contaminated by DON. The initial DON content in raw wheat largely determines the DON content in wheat processing products; however, proper processing may reduce DON concentration, considering that DON mainly accumulates in the bran layer. Compared with raw grains, processed food products generally present less DON contamination. The stability of DON under food handling conditions should be evaluated.

The change in DON content can be explained by the movement or dilution of DON, as well as the transformation of DON or its derivative and precursor. Food processing techniques, including sorting, cleaning, pearling, milling, baking, heating, frying, kneading, fermentation, cooking, influence DON content. They are mainly divided into the physical processing of raw grains, addition and blending of food additives and other ingredients, and chemical processing of intermediate or semi-finished products. DON may decrease during handling; however, the effects of processing on DON are complex and at times inconclusive. Critical influencing factors include temperature, heating time, enzymes, yeast, location of DON, food composition, and size of food.

Our analysis shows that the different fates of DON could be partly attributed to the following reasons: (a) the method used to calculate the DON degradation rate; (b) recovery factors and food matrix; (c) food size; (d) method selected for mycotoxin detection (Table S2); and (e) cereal raw materials (for example, spring wheat and durum wheat) and food processing techniques.

3.1 | Bread making

Bread provides carbohydrates, proteins, fat, vitamins, and minerals and is widely consumed globally. Meanwhile, bread is mainly made from wheat and may be the major contributor to DON exposure. The fate of DON may be difficult to determine during bread making but is significant. A flowchart for bread making is presented in Figure 1. Most reports on how processing influences mycotoxins emphasize the effect of fermentation and baking.

3.1.1 | Wheat processing

Grain processing starts with the removal of dust, poor-quality grains, and foreign material. Primary processing of wheat mainly includes cleaning, sorting, conditioning, dehulling, and milling. All these processes have been reported to reduce DON content. Meanwhile, most of the data relate to the milling and cleaning stages. The water solubility of DON may lead to the movement and reduction of DON in the final flour. Notably, the DON loss in flour preparation is related to raw wheat. DON shows increased mobile activity in grains.

Mycotoxins are usually distributed unevenly in grains, and this can be related to the limited ability of toxin producing fungi to penetrate the grain shell. DON is mostly concentrated in the bran and outer layers, and its location is crucial for DON reduction. Studies for accumulation of DON in grain revealed consistent distribution trends of different parts of grains. Compared with the inner parts (endosperm and flour), the parts near the outer layer (bran, shorts, and hulls) present high level of DON. Another review regarding distribution of mycotoxins in wheat confirmed the distribution law from the side, because DON level in wheat by-products (bran, middling, shorts, and screenings) increased up to seven times compared to the original wheat (Cheli, Pinotti, Rossi, & Dell'Orto, 2013).

According to the correlation analysis of the total toxin level in the whole grains and the sum of the toxin level in different fractions, the inequal accumulation trend was demonstrated to be natural distribution, which was not caused by the operation of grain treatment. In oat samples, more than 50% of the DON content in the original whole grains was detected in hulls, whereas relatively low level of DON was found in oat kernels, pearling fractions, and remaining kernels. Content of DON was 201 to 1,636 μg in whole grain, 155 to 1,197 μg in hulls, and 0.81 to 105 μg in kernels (Ivanova et al., 2017). In wheat kernel regions, DON content in bran (8.3 to 122 mg/kg) was about six times that of break flour (1.4 to 16.2 mg/kg), and in shorts (6.4 to 84.4 mg/kg) about three times that of break flour (2.5 to 16.2 mg/kg) (Gärtner, Munich, Kleijer, & Mascher, 2008). In barley kernel region (roller milling), the hull enriched fractions contained about three to six times more DON than the endosperm enriched fractions. Level of DON in hull fractions was in the range of 71.3 to 109.0 μg/kg, and in endosperm fractions was in the range of 9.4 to 35.5 μg/kg (Khatibi et al., 2014).

Besides, the distribution of DON in grains may be related to varieties. For example, in BRS 374 wheat, bran fractions and milled wheat presented similar content of DON, which was two times of DON than flour. However, in BRS Parrudo wheat, level of DON was similar in bran fractions and flour (Tibola, Fernandes, & Guarienti, 2016).

Primary processing procedures such as sorting and cleaning significantly reduce DON in the early stages because contaminated grains or low-density grains can be removed. The amount of DON reduced by cleaning varied from 7% to 50% (effect of cleaning, sorting, and milling in wheat mycotoxin content). In addition, milling, pearling, and dehulling have effectively reduced DON (Vidal, Marín, Morales, Ramos, & Sanchis, 2014; Vidal, Morales, Sanchis, Ramos, & Marín, 2014; Vidal, Sanchis, Ramos, & Marín, 2015, 2016; Suman & Generotti, 2015). Milling is a process of crushing grain into flour. In this study, DON content decreased by nearly

TABLE 2 Effects of food processing on DON content

Type of food	Processing method	Effects on DON	Reference
Wheat	Milling	Reduction of 36.7% (roller mill) to 85.1 % (precision mill system)	Khatibi et al., 2014
Wheat	Cleaning	Reduction of 500 to 3,000 µg/kg	Tibola et al., 2016
Wheat	Cleaning	Reduce 20% to 30%	Kostelanska et al., 2011
Wheat	Milling	Reduce 62%	Kostelanska et al., 2011
Wheat	Milling	Reduction 22%	Edwards et al., 2011
Wheat	Dry milling	50% in bran/germ, 42% in semolina	Magallanes López, Manthey, & Simsek, 2019
Wheat	Wet milling	Reduced to undetectable levels	Magallanes López et al., 2019
Bread	Dough preparation	Reduction of 7% without sourdough and increase of 24% with sourdough	Vidal, Marín, et al., 2014
Bread	Dough preparation (proofing, kneading)	No significant change	Kostelanska et al., 2011; Wu & Wang, 2015
Bread	Fermentation	No significant change	Kostelanska et al., 2011; Wu & Wang, 2015
Bread	Fermentation	Slight increase	Bergamini et al., 2010
Bread	Fermentation without enzymes	Decrease 5% at 30 °C, 23% at 45 °C	Vidal et al., 2017
Bread	Fermentation with enzymes	Increase 10% (30 °C, a-amylase), 15% (xylanase), 63% (cellulase), 75% (protease), and 78% (glucose–oxidase)	Vidal et al., 2017
Bread	Fermentation with nonspecial enzymes	Increase 14%	Suman, Manzitti, & Catellani, 2012
Bread	Fermentation with enzyme	Increase 99%	Simsek et al., 2012
Bread	Fermentation	Increase 30%	Vidal, Morales, et al., 2014
Vienna bread	Fermentation	Reduce 0% to 56%	Samar et al., 2001
French bread	Fermentation	Reduce 0% to 41% at 50 °C	Samar et al., 2001
Bread	Fermentation	Reduce 21.6%	Neira, Pacin, Martinez, Moltó, & Resnik, 1997
Bread	Fermentation	Reduce 38% to 46%	Lancova, Hajslova, Poustka, et al., 2008
Bread	Baking	Reduce 28.9%	Neira et al., 1997
Bread	Baking	Decrease 4% to 14%	Wu & Wang, 2015
Bread	Baking	Decrease 13%	Kostelanska et al., 2011
Bread	Baking (200 °C, 15 min)	Decrease 2%	Stadler et al., 2019
Bread	Baking	Decrease DON only in highly contaminated raw material	Bergamini et al., 2010
Bread	Baking	Decrease 29% to 89%	Vidal et al., 2015
Bread	Baking without enzymes	Reduce by 10.97%	Vidal et al., 2017
Bread	Baking	Reduce 29% to 81%	Vidal et al., 2015
Bread	Baking	Decrease 8% to 19%	Generotti et al., 2015
Bread	Toasting	Decrease 19% to 65%	Generotti et al., 2015
Bread	Baking	Reduce 7%	Boyacioğlu et al., 1993
Bread	Baking	Reduce 40%	Vidal et al., 2018
Turnover pie dough covers	Frying	Reduce 28%, 21%, and 20% at 169, 205, and 243 °C, respectively	Samar, Resnik, Gonzalez, Pacin, & Castillo, 2007
Crackers	Baked at 250 °C for 5 min and dried at 100 °C for 30 min	Decrease 6%	Stadler et al., 2019

(Continues)

TABLE 2 (Continued)

Type of food	Processing method	Effects on DON	Reference
	Fermentation with enzyme	Increase 14%	Suman et al., 2012
Biscuits	Baking	Decrease 5%	Stadler et al., 2019
Biscuits	Baking	Reduce 9% to 68%	Generotti et al., 2017
Cocoa biscuit	Baking	Reduce 17% to 68%	Generotti et al., 2017

100%. Different mill systems resulted in different reduction rates. Precision mill systems (85.9 %) were reportedly more effective in reducing DON, compared with roller mill systems (36.7%). Relative data are collected in Table 2. DON is not destroyed during cleaning, milling, and dehulling; instead, it is redistributed. DON is mostly redistributed during removal or is dissolved in water. One problem caused by these strategies is the loss of cereal mass, particularly starch. Accordingly, dehulling methods that are more effective and less costly are being developed.

3.1.2 | Dough preparation

Dough preparation includes kneading, fermentation, and proofing. Published data on the fate of DON during bread fermentation largely vary. Our analysis indicates that DON content was significantly influenced by enzymes, ingredients, and fermentation condition. Some studies have found that fermentation exerts no significant influence on DON as reported by Wu and Wang (2015) and Cano-Sancho, Sanchis, Ramos, and Marín (2013). Other studies have shown contradictory results (Bergamini et al., 2010; Lancova, Hajslova, Kostelanska, et al., 2008). In the current study, DON was reduced or significantly increased during fermentation, which was markedly influenced by the presence of ingredients, such as enzymes, flour improvers, and malt flour. The increase in DON may be attributed to the release of DON. An increase in DOM-1 during fermentation may be explained by the transformation of DON.

Enzyme activities during bread making should be investigated, considering the effects of enzymes. Several studies on enzymes and improvers have consistently reported that enzymes lead to the increase of DON during fermentation. This finding can be explained by the release of DON from the food matrix. Studies have found that the following have induced an increase in DON: α-amylase (Simsek, Burgess, Whitney, Gu, & Qian, 2012); cellulase, α-amylase, protease, xylanase, and glucose-oxidase (Arnau Vidal, Sanchis, Ramos, & Marín, 2017); flour improvers (Vidal, Morales, et al., 2014); and xylanase, α-amylase, and cellulase (Vidal, Sanchis, et al., 2016; Vidal, Ambrosio, Sanchis, Ramos, & Marín, 2016).

Fermentation temperature may be another factor affecting DON stability. Studies have reported a decrease in DON content during fermentation without enzymes, with the decrease rate determined by the fermentation temperature; the higher the temperature, the more conducive to DON degradation (Samar, Neira, Resnik, & Pacin, 2001; Vidal et al., 2017). Bread fermented at 30, 40, and 50 °C showed that optimal reduction occurred at 50 °C with the longest fermentation time (Samar et al., 2001). Similarly, DON reduction increased with a rise in temperature from 30 to 45 °C and from 26 to 46 °C (Wu & Wang, 2015; Vidal et al., 2017). Interestingly, Bergamini et al. (2010) and Vidal, Morales, et al. (2014) observed an increase in DON when no enzymes were added.

During fermentation, D3G decreased slightly, but DOM-1 increased. A higher increase in DOM-1 was observed at 30 °C than at 45 °C. We speculate that DON was converted into DOM-1. The transformation of masked forms and free DON during fermentation needs to be further identified.

3.1.3 | Baking

Baking is one of the key and characteristic processes of bread making. Its effects on DON content have been evaluated in a large number of studies. The key parameters in this handling process include initial contamination level, baking time, temperature range, food additives, water content, enzymes, and size of bread. Regardless, our statistics indicate that results largely varied. After baking, the change in DON level ranged from an increase of more than 90% to a decrease of 89%.

Conversion between DON and its modified forms have also attracted attention. Heating under alkaline conditions has degraded DON into norDON (Bretz, Beyer, Cramer, Knecht, & Humpf, 2006). Chemical reactions have occurred during baking. DON may be transformed into isoDON, DOM1, norDON A, norDON B, norDON C, norDON D, norDON E, norDON F, and 9-hydroxymethyl DON lactone (hy-DON-lac), among others. Reports on the transformation of DON during baking remain incomplete. Most studies have assumed that the degradation of DON during baking leads to a reduction in toxicity. Further studies are needed to confirm whether the already known degradation products will still be transformed, and whether matrix entrapment and bound forms will occur (Stadler et al., 2019). The degradation of DON in baking cannot be determined merely by detecting a decrease in DON concentration. Moreover, the mechanisms underlying the considerable increases in D3G (>80 %) and DOM-1 (>20 %) during baking need to be identified. Whether the

increase in D3G is related to the conversion of DON has to be determined.

Some studies showed that DON was relatively stable and its content slightly changed during baking. This result could be partly attributed to the high-temperature resistance of DON. Moreover, some studies detected the highest reduction in samples with high contamination (high concentration) (Bergamini et al., 2010; Vidal et al., 2015, 2017). The initial concentration of DON was thus considered as a factor influencing DON content.

Interestingly, contrary findings showed that DON content changed was largely due to baking (Lancova, Hajslova, Poustka, et al., 2008; Scudamore, Hazel, Patel, & Scriven, 2009; Valle-Algarra et al., 2009; Vidal et al., 2015). Baking time was considered a significant factor affecting DON content and in some cases was more influential than baking temperature (Lancova, Hajslova, Poustka, et al., 2008; Scudamore et al., 2009; Vidal, Morales, et al., 2014).

The results were rather inconclusive for baking temperature. One study considered baking temperature as a crucial factor (Vidal et al., 2015), whereas another study found it negligible (Generotti et al., 2015). The latter found that that fermentation temperature was considerably more crucial than baking temperature in reducing DON. DON was converted into isoDON, norDON B, and norDON C during baking of bread, crackers, and biscuits (Stadler et al., 2019). In bread, DON was reduced by 2%. The same study indicated that the similar transformation of DON in three different foods indicated that the DON degradation mechanism was independent of baking conditions and formulations. Meanwhile, norDON A, norDON B, norDON C, and norDON F were found in bread crust, and the conversion of 3-ADON and 15-ADON to DON was analyzed (Wu & Wang, 2015). In a study by Kostelanska et al. (2011), degradation products, including norDON A, norDON B, norDON C, norDON D and DON lactone, were mainly located in bread crust. This finding agreed with the hypothesis that DON degradation mainly occurred in the outer layers of bread, which rapidly reaches high temperature. Thus, bread size also affected DON during baking.

Food additives such as potassium bromate and L-cysteine did not change DON content in postbaking; however, sodium bisulfite, L-cysteine, and ammonium phosphate reduced DON by 40% (Boyacioğlu, Heltiarachchy, & d'appolonia, 1993). Boyacioğlu et al. (1993) evaluated the effect of oxidizing and reducing agents on DON. Sodium bisulfite, L-cysteine, and ammonium phosphate facilitated DON reduction during baking. Additives alter pH. Although DON is sensitive to changes in pH, DON reduction is independent to such changes (Vidal, Sanchis, Ramos, & Marín, 2018).

Interestingly, several studies compared the thermal stability of DON in food matrixes and standard solutions under the same processing conditions simultaneously. It seems that DON was more stable in real food samples than in standard solutions. As to the different degradation activities of DON between standard and real food samples, the reasons may include the interaction between DON and food components, and the thermal barrier effect of food matrix (Samarajeewa, 1991).

Generally, temperature above 150 °C was effective in reducing DON in standard. Besides, the thermal degradation rate of DON was affected by the pH of DON standard solutions, because strong alkaline conditions promoted the degradation of DON. When heated at 140, 160, 180, 200, or 220 °C by a convection oven, both DON standards and naturally contaminated whole barley power showed a time- and temperature-dependent degradation of DON. The highest temperature led to the most effective degradation result. The times required to reduce 50% or 90% of DON were similar. However, the degradation rate for standard solution was twice as high as that of the barley power. When heated for 60 min, 100%, 96%, 79%, 48%, and no more than 15% of DON were reduced in DON standard at 220, 200, 180, 160, and 140 °C, respectively (Yumbe-Guevara, Imoto, & Yoshizawa, 2003). Another study using laboratory dryer (160 °C, 30 min) for heating identified most of the already known thermal degradation products of DON in DON standard solutions, including norDON A-F, DON lactone, isoDON, and 9-OH DON lactone. However, less kinds of degradation products were detected in bread samples, including norDON A, B, C, D, F, and DON lactone (Kostelanska et al., 2011). Other studies also confirmed the thermal decomposition of DON in standard solutions, as shown in Table S3.

It is worth noting that several studies observed the inconsistent thermal stability of DON in standard because of the different analysis methods. For example, when DON standard was heated at 150 °C for 10 and 20 min, a slight increase of DON (5% to 8%) was detected by ELISA, whereas a mild reduction (<21%) of DON was observed by gas chromatography–mass spectrometry. This can be explained that DON derivates produced during heating performed stronger cross-reactivity than DON against the antibody (Blanca, Guevara, & Yoshizawa, 2004).

Meanwhile, DON was reduced without enzymes during baking, and the presence of α-amylase and xylanase limited DON reduction. The reduction depended on the fermentation temperature (Vidal et al., 2017). The toxicity of certain degradation productions of DON has been studied. For instance, norDON A, norDON B, and norDON C of up to 100 μmol showed no significant effects (Bretz et al., 2006; Vidal et al., 2017).

The kinetics of DON degradation during wheat baking or maize bread baking has been studied (Numanoglu, Gökmen, Uygun, & Koksel, 2012; Vidal et al., 2015), which can be useful for DON degradation during food processing. The dynamic model exhibited a good fit.

3.2 | Baby food

Baby has a single diet mainly consisting of grains and milk, such as wheat, oats, barley, and rice. Recent studies have revealed DON contamination in grain-based baby food. The positive detection rate exceeds 50%, contamination level ranging from 13 to 160.6 μg/mL (Cano-Sancho, Gauchi, Sanchis, Marín, & Ramos, 2011; Juan, Raiola, Mañes, & Ritieni, 2014; Pereira, Fernandes, & Cunha, 2015; Oueslati, Berrada, Manes, & Juan, 2018). Owing to incomplete development, high metabolite rate, and weak resistance, infants are highly vulnerable to mycotoxins. Effects of toxicity manifest within hours in children (Raiola, Tenore, Manyes, Meca, & Ritieni, 2015). Thus, it is necessary to investigate the fate of DON particularly during baby food processing. Figure 5 shows the processing of baby food.

Our review of studies reveals that only one examined the effects of baby food processing on DON content. DON content was considerably reduced by dehulling, roasting, fermentation, soaking, and blanching. For the same kind of food, the reduction rate was influenced by different processing methods. The emergence of masked forms in the final products or intermediate products, such as D3G and 3-ADON, presented an additional risk.

During ogi processing, leaching and the microorganisms used for fermentation are potentially responsible for DON content. Fermentation and wet milling significantly reduced DON content by 30% to 66%; the later reduced DON to an undetectable level. Transformation of DON to D3G was indicated. During soybean powder processing, DON was reduced by 44% to 66% by roasting and by 66% to 77% by soaking and blanching (Chilaka, De Boevre, Atanda, & De Saeger, 2019).

4 | DEGRADATION OF DON BY MICROORGANISMS

Figure 6a shows the development of microbial strategies for mycotoxin control. For a comprehensive study on the microbial detoxification of mycotoxins, six study progresses are expected to be conducted (Figure 6b). The toxicity of both the microorganisms and DON degradation products should be evaluated and be considered as an index to assess the suitability of the detoxification methods. In view of the safety of food production, hazard characterization should be performed prior to the commercial application of the detoxification methods.

4.1 | Mechanism of DON biodegradation

To evaluate DON degradation, an in-depth understanding of the biodegradation mechanism of DON is a prerequisite. The biodegradation mechanism of DON can be mainly divided, based on its chemical structure, into adsorption and transformation. Comprehensive analysis of more than 100 papers published in this field indicates that the biotransformation pathways of DON can be divided into the following modes: oxidation, acetylation, glycosylation, hydroxylation, isomerization, and hydrolysis. Biological oxidation mainly occurs at C-3 and C12/C13 of DON. The degradation product 3-keto-DON is produced when the 3-OH functional group is oxidized into the 3-keton group by hydroformylation. DOM-1 is produced via deepoxidation of the C12/C13 epoxy group. Several studies have elaborated on the biological reactions of trichothecene mycotoxins (He, Zhou, Young, Boland, & Scott, 2010; Karlovsky, 2011). The present study discusses DON biodegradation from the perspective of microorganisms in the subsequent content.

Microorganisms detoxifying DON mainly consist of bacteria and fungi. Research on animal digestive bacteria to detoxify DON dates back to 1983. In this study, these microorganisms are divided into lactic acid bacteria, bacteria from soil, bacteria from plants, other rumen and intestinal microbes, yeast, and molds. With regard to microorganisms, animals, or enzymes, the degradation mechanisms can be divided into (a) inhibition of fungal growth, (b) inhibition of the production of DON independent of the inhibition of fungi, (c) binding or adsorption of DON, (d) transformation of DON, and (e) enhancement of the resistance to DON (Figure 1). Generally, research has witnessed the evolution of DON biodegradation from anaerobic degradation to aerobic degradation, as well as from mixed flora to pure cultures. Sources of biotransformation microorganisms include the environment (particularly soil and water), plants (Ito et al., 2012), insects, and animals (Zhu, Hassan, Lepp, Shao, & Zhou, 2017). Mycotoxins do not accumulate in farmland soil; soil and water bodies are supposed to be good sources of mycotoxin-detoxifying microorganisms (Sato et al., 2012; Völkl, Vogler, Schollenberger, & Karlovsky, 2004).

All aforementioned organisms for DON detoxification are discussed in this study. Isolation of microorganisms from an environment similar to the subsequent practical application environment is suggested. Thus, the isolated microbe would grow better and show a higher detoxification activity (Zhu et al., 2017). Table 3 presents the organisms of various resources that counteract DON.

The biotransformation products mentioned in this review mainly include DOM-1, D3G, 3-keto-DON, and 3-epi-DON. Published reports on the toxicity evaluation of degradation products are summarized in Table 4.

4.2 | Degradation of DON by bacteria

Bacteria are the most studied organisms for DON detoxification. Bacteria such as lactic acid bacteria and other

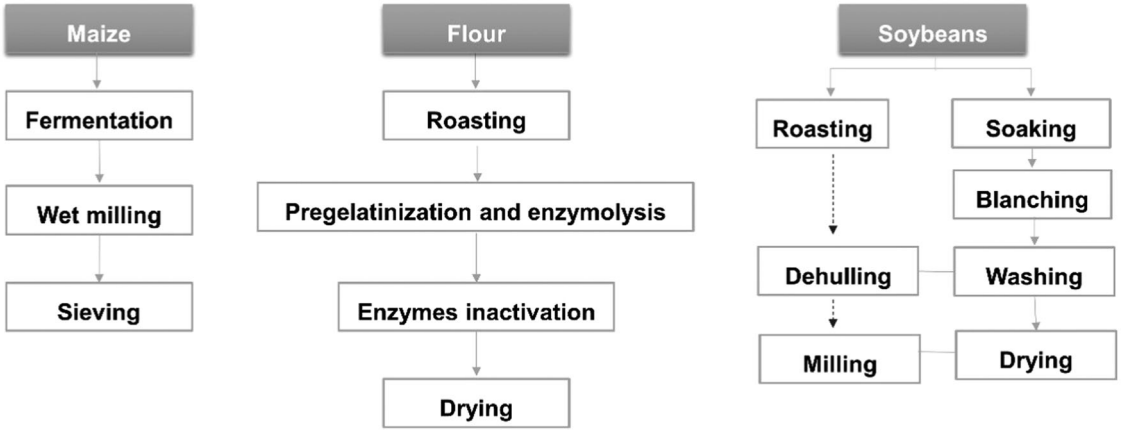

FIGURE 5 Processing of different baby foods. Adapted from Chilaka et al. (2019) and Pascari, Marín, Ramos, Molino, and Sanchis (2018)

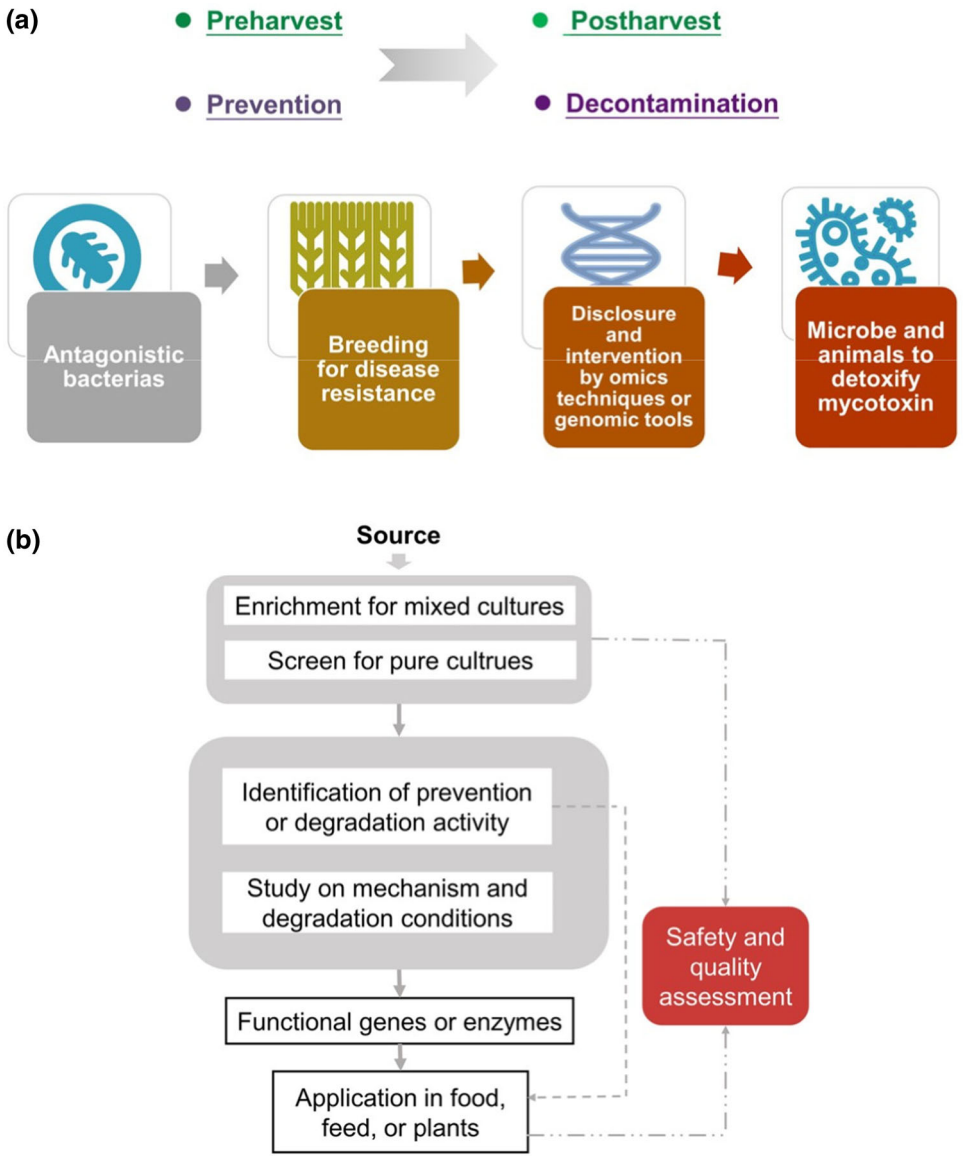

FIGURE 6 Biological degradation for mycotoxins. (a) Development of biological control strategies for mycotoxins. (b) Procedure for the systematic and comprehensive investigation of microbial detoxification of mycotoxins

TABLE 3 Microorganisms that can detoxify DON

Species	Strain or microbial community	Degradation mechanism	Degradation product	Reference
Lactic acid bacteria	*Enterococcus*	Binding DON	–	Niderkorn et al., 2007
	Lactobacillus plantarum, *Lactobacillus pentosus*, and *Lactobacillus paracasei*	Inhibiting fungal growth, adsorbing DON	–	Franco et al., 2011
	Lactococcus lactis, *Lactobacillus brevis*, *Lactobacillus casei*, *Lactobacillus plantarum*, and *Lactobacillus plantarum*	Binding DON	–	Zou et al., 2012
	Lactobacillus sp.	Binding DON	–	Chlebicz & Śliżewska, 2019
	Three *Pediococcus pentosaceus* strains	Antifungal activity, binding or transforming DON	–	Juodeikiene et al., 2018
	Lactobacillus rhamnosus RC007	Mild degradation of DON, reduction of all effects of DON on pig jejunum explants	–	García et al., 2018
	Lactobacillus plantarum JM113	Antioxidant activity, protecting the integrity of the intestinal barrier	–	Yang, Li, et al., 2017
Other rumen and intestinal microflora	Microbial inocula from rumen and intestines of chicken	Oxidation	DOM-1	He et al., 1992
	Eubacterium sp. strain BBSH 797	Oxidation	DOM-1	Fuchs et al., 2002
	Microbiota and pure cultures of bacteria obtained from chicken intestine	Oxidation	DOM-1	Young et al., 2007
	Bacillus spp., Clostridiales, *Anaerofilum* sp., *Collinsella* sp.	Oxidation	DOM-1	Li et al., 2011; Yu et al., 2010
	Human fecal microbe	Oxidation	DOM-1	Gratz et al., 2013
	Eggerthella sp. DII-9	Oxidation	DOM-1	Gao et al., 2018
	Fish digesta	Oxidation	DOM-1	Guan et al., 2009
Bacteria from soil	*Agrobacterium–Rhizobium* strain E3-39	Oxidation	3-keto-DON	Shima et al., 1997
	WSN05-2	Isomerization	3-epi-DON	Ikunaga et al., 2011
	Paenibacillus polymyxa	Inhibiting fungal growth and production of DON	–	He et al., 2009
	Devosia mutans 17-2-E-8	Oxidation, Isomerization	3-keto-DON, 3-epi-DON	He et al., 2015, 2016
	Devosia sp. ANSB714	Eliminating effects of DON on mice and pig, decreasing DON residues	–	Li et al., 2018; Zhao et al., 2016
	Devosia sp. DDS-1	Oxidation	3-keto-DON	Xu et al., 2010
	Devosia insulae A16	Oxidation	3-keto-DON	Wang et al., 2019

(Continues)

TABLE 3 (Continued)

Species	Strain or microbial community	Degradation mechanism	Degradation product	Reference
	Enrichment cultures	Isomerization, oxidation	3-epi-DON, DOM-1	Vanhoutte et al., 2018
	Nocardioides, genus *Devosia*	Isomerization	3-epi-DON and other metabolites	Sato et al., 2012
	DX100	Oxidation	DOM-1	Ahad et al., 2017
Bacteria from plants	*B. amyloliquefaciens* WPS4-1 and WPP9	Inhibiting fungal growth or/and synthesis of DON	–	Shi et al., 2014
	Brevibacillus sp. BRC263, *Streptomyces* sp. BRC87B	Inhibiting production of DON	–	Palazzini et al., 2007
Yeast	*Saccharomyces pastorianus* A15	Glycosylation	D3G	Nathanail et al., 2016
	Saccharomyces cerevisiae	Binding DON	–	Campagnollo et al., 2015; Chlebicz & Śliżewska, 2019
	Saccharomyces cerevisiae boulardii	Counteracting DON toxicity in piglets	–	Alassane-Kpembi et al., 2018
	Lachancea thermotolerans volatile organic compounds	Inhibiting fungal growth and DON synthesis	–	Zeidan et al., 2018
	Yeast cell wall product	Adsorbing DON	–	De Souza et al., 2014; Kong et al., 2014; Patience et al., 2014
	Geotrichum fermentans, *Kluyveromyces marxianus*, *Metschnikowia pulcherrima*	Not mention	–	Repečkienė et al., 2013
Mold	*Aspergillus tubingensis*	Hydrolysis	Molecular weight was 314.4	He et al., 2008
	Aspergillus oryzae	Absorbing DON	–	Garda-Buffon et al., 2011
	Rhizopus oryzae	Absorbing DON	–	Garda-Buffon et al., 2011

miscellaneous bacteria from soil, water, plants, the rumen, and the intestines have shown the ability to detoxify DON, and some degradation products have been identified. Both anaerobic and aerobic microorganisms have been developed. Exploration and characterization of DON-degrading bacteria may provide precise choices for bacterial strains and procedures for in situ detoxification. The processes provide insights into the diversity of degrading strains and how they are degraded in the environment (Ikunaga et al., 2011). Moreover, probiotics have been identified by FAO/WHO as microbes that can bind and absorb mycotoxins (FAO/WHO, 2002). The utilization of bacteria may be a promising method for DON degradation in situ.

4.2.1 | Rumen microbes and intestinal microflora

Rumen fermentation is the first line of defense toxic tort in vivo. Tumor gastric juice and intestines are hosts of multiple microbial communities. Moreover, ruminants are less sensitive to mycotoxins, particularly trichothecenes, suggesting the potential of rumen fluid and intestines for biotransformation (Swanson et al., 1987; Tan et al., 2015). Microorganisms from the rumen and the intestines have shown the ability to degrade DON by deepoxidation. Studies on these bacteria are mainly conducted under anaerobic conditions.

Research on the use of rumen microflora to detoxify DON began early. In vitro transformation of DON by rumen or gut

TABLE 4 Toxicity of major DON biotransformation products

Toxin	Evaluation model	Toxic effect	Reference
3-epi-DON	Caco-2 cell	IC_{50} was 357 times higher than that of DON	He et al., 2015
	Caco-2 cell	Not cytotoxic, neither changed oxygen consumption nor impaired barrier function	Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016
	3T3 fibroblasts cell	IC_{50} was 1,181 times higher than that of DON	He et al., 2015
	Intestinal explants	No intestinal lesions were observed	Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016
	Female B6C3F1 mice	No effects on body and organ weights, hematology, and organ histopathology	He et al., 2015
3-keto-DON	Caco-2 cell	IC_{50} was 3.03 times higher than that of DON	He et al., 2015
	Fibroblasts NIH/3T3 cell	IC_{50} was 4.54 times higher than that of DON in BrdU assay	He et al., 2015
	Mouse spleen lymphocyte	Immunosuppression by 3-keto-DON was 90% lower than that of DON	Shima et al., 1997
DOM-1	Bovine ovarian theca cell	Inhibited progesterone and testosterone secretion, increased apoptosis	Guerrero-Netro et al., 2017
	HepG2 cells	Decreased albumin secretion	Mayer et al., 2017
	Chicken lymphocyte	500 times less toxic than DON	Sundstøl Eriksen & Pettersson, 2003
	Mouse fibroblast	54 times less toxic than DON	
	3T3 cell	IC_{50} was 54 times higher than that of DON	Eriksen et al., 2004
	Bovine peripheral blood mononuclear cells (PBMC)	Reached the maximum inhibition of approximately 24% at the concentration of 18.29 μM	Daenicke et al., 2011
	Holstein cows	Exposure of dairy cows resulted in maximum serum DOM-1 level of 52 ng/mL	Daenicke et al., 2011
	PBMC	No effect on the viability to concentration 23 μM	Dänicke et al., 2010
	IPEC-1		
	IPEC-J2		
	Caco-2 cell	Not cytotoxic, neither changed oxygen consumption nor impaired barrier function	Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016
	Intestinal explants	No intestinal lesions were observed	Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Schatzmayr, et al., 2016
D3G	GES-1 cells	No toxicity	Yang, Yu, et al., 2017
	Caco-2 cells	Unable to bind to the A-site of the ribosome peptidyl transferase center, did not alter viability and barrier function	Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Liaubet, et al., 2016
	Porcine jejunal explants	Induced no histomorphologic alterations	Pierron, Mimoun, Murate, Loiseau, Lippi, Bracarense, Liaubet, et al., 2016
	Chlamydomonas reinhardtii	Caused no cell growth inhibition, induced limited DNA differences	Suzuki & Iwahashi, 2015
	Porcine intestinal epithelial cell	No apoptosis	Broekaert et al., 2016
	Mouse	Induced no reaction of chemokine splenic or cytokine mRNA	Wu, He, et al., 2014
	Mice	Unable to stimulate pro-inflammatory cytokines, weakened ability to elicit gut satiety peptides and anorectic responses	Wu, Zhou, et al., 2014

microflora was conducted extensively (He, Young, & Forsberg, 1992; King, McQueen, Levesque, & Greenhalgh, 1984; Kollarczik, Gareis, & Hanelt, 1994; Swanson et al., 1987). Under anaerobic conditions in vitro, microbial inocula from the rumen and the intestines of chicken convert DON to DOM-1. He et al. (1992) demonstrated that the degradation activity was maintained through six serial subcultures. Binder et al. (1997) isolated the first pure transforming microorganism used for DON detoxification. Fuchs, Binder, Heidler, and Krska (2002) confirmed that the isolated culture, *Eubacterium* sp. strain BBSH 797, from rumen anaerobically transformed DON into DOM-1. Young et al. (2007) also verified that microbiota and pure cultures of bacteria obtained from chicken intestines degraded DON into DOM-1. Ten isolated strains were further identified, including *Bacillus* spp., Clostridiales, *Anaerofilum* sp., and *Collinsella* sp. (Li et al., 2011; Yu et al., 2010). Reports on the metabolic assessment of DON by human microorganisms remain inadequate. Gratz et al. (2013) observed that human fecal microbes anaerobically detoxify DON into DOM-1 in vitro. *Eggerthella* sp. DII-9, a novel deepoxidation bacterium from chicken intestines, was reported to have effectively transformed DON into DOM-1 (Gao et al., 2018). Intestinal microorganisms from bovine rumen fluid, dairy cattle, pigs, rats, sheep, and fish digesta were able to convert DON (Côté, Dahlem, Yoshizawa, Swanson, & Buck, 1986; Cote, Nicoletti, Swanson, & Buck, 1986; Guan et al., 2009; King et al., 1984; Kollarczik et al., 1994; Westlake, Mackie, & Dutton, 1989; Yoshizawa, Takeda, & Ohi, 1983).

Commercial products, such as Biomin® BBSH 797 containing biotransform agents, have also been developed and patented as feed additives (EFSA, 2005). Biomin® BBSH 797 is the first microorganism authorized by the European Food Safety Authority that converts trichothecenes into less toxic metabolites for poultry and swine diets (Rychen et al., 2017). This microorganism can convert DON into DOM-1. In vitro and in vivo studies have indicated that Biomin® BBSH 797 at the recommended level can effectively reduce DON. However, at the time the studies were conducted, Biomin® BBSH 797 was not available in the United States or Canada.

4.2.2 | Bacteria from soil

Several studies have been conducted on the degradation of DON by aerobic bacteria. Shima et al. (1997) isolated the *Agrobacterium–Rhizobium* strain E3-39 from soil for DON detoxification. Strain E3-39 completely transformed DON into 3-keto-DON under aerobic conditions after incubation for one day. The modified mycotoxin 3-acetyldeoxynivalenol can also be transformed by strain E3-39. The strain WSN05-2, identified as the *genus Nocardioides* and isolated from wheat soil, completely degraded 1,000 μg/mL of DON in a culture medium under aerobic conditions after 10 days. DON in wheat grain was also reduced by approximately 90% after 7 days. The intermediate 3-epi-DON was first reported in this study (Ikunaga et al., 2011). *Paenibacillus polymyxa* also inhibited the growth of *F. graminearum* and the production of DON under greenhouse conditions (He, Boland, & Zhou, 2009). He et al. (2015) and He et al. (2016) observed that *Devosia mutans* 17-2-E-8 from soil completely converted DON into the major metabolite 3-keto-DON and the secondary metabolite 3-epi-DON under aerobic conditions. Carere, Hassan, Lepp, and Zhou (2018) and Hassan et al. (2017) investigated the relevant enzymatic mechanism underlying epimerization. Similarly, enrichment cultures from a maize field and a wastewater treatment plant, a microbial community with at least six bacterial genera, 13 aerobic bacteria from soil and wheat leaves belonging to the genera Nocardioides and Devosia, a microbial consortium called DX100 from soil, *Devosia* sp. ANSB714 from soil, and *Devosia* sp. were screened. Meanwhile, DDS-1 was able to detoxify DON (Ahad, Zhou, Lepp, & Pauls, 2017; Sato et al., 2012; Vanhoutte, Audenaert, & De Gelder, 2018; Xu et al., 2010; Zhao et al., 2016; Zhu et al., 2017). Karlovsky suggested that microorganisms such as *Curtobacterium* sp. 114-2, *Pseudotaphrina kochii*, *Agrobacterium–Rhizobium* E3-39, *Nocardioides* sp. WSN05-2, and so on can also be used as feed additives (Karlovsky, 2011).

4.2.3 | Lactic acid bacteria

The most prevalent method to reduce mycotoxin exposure is to use a binder and adsorbents to decrease the bioavailability of mycotoxins (Hathout & Aly, 2014). The superiority of microbial adsorption is evident considering that they do not negatively affect nutritional quality, and the reaction condition is mild. Published reports identify fungi and lactic acid bacteria as the most widely studied microorganisms capable of absorbing DON. However, the ability of some microorganisms to bind to DON was not as strong as that of ZEN, AF, and so on. Significant challenges include the effectiveness of microorganisms under different pH levels and that stability of mycotoxin-absorbent complex products.

Since the birth of agriculture, lactic acid bacteria have been used to preserve food. Lactic acid bacteria are anaerobic, and some can tolerate low levels of oxygen. In addition, lactic acid bacteria improve the flavor, texture, and shelf life of foods and play an important role in global food production. These foods include dairy products, vegetables, meat, and many indigenous fermented foods, among others (Indira, Jayalakshmi, Gopalakrishnan, & Srinivasan, 2011; Nuraida, 2015; Perczak, Goliński, Bryła, & Waśkiewicz, 2018; Wood, 2012; Zannini, Waters, Coffey, & Arendt, 2016). Lactic acid bacteria exhibit the greatest potential for inhibiting fungal growth and detoxifying mycotoxins (Gourama & Bullerman,

1995; Hocking, Pitt, Samson, & Thrane, 2006). The ability to inhibit fungal growth may be attributed to the competition of nutrients, production of antagonistic substances, and production of organic acids (Magnusson & Schnürer, 2001; Magnusson, Ström, Roos, Sjögren, & Schnürer, 2003; Niku-Paavola, Laitila, Mattila-Sandholm, & Haikara, 1999; Schnürer & Magnusson, 2005). Detoxification may arise from metabolism, adsorption of the cell structure, or degradation (Dalié, Deschamps, & Richard-Forget, 2010; García et al., 2018; Haskard, El-Nezami, Kankaanpää, Salminen, & Ahokas, 2001; Shetty & Jespersen, 2006).

A total of 202 strains of fermentative bacteria, including *Lactobacillus* spp., *Enterococcus*, *Lactococcus*, *Leuconostoc*, *Pediococcus*, *Propionibacterium*, and *Streptococcus*, were screened to evaluate their ability to bind or transform mycotoxins (DON\ZEN\fumonisins) in vitro. Most strains were able to bind DON, with *Enterococcus* as the most effective strains (Niderkorn, Morgavi, Pujos, Tissandier, & Boudra, 2007). Franco, Garcia, Hirooka, Ono, and Santos (2011) determined that three isolated lactis inhibited the growth of *F. graminearum* IAPAR 2218 and removed DON. The strains *L. plantarum*, *L. pentosus*, and *L. paracasei* absorbed 67%, 47%, and 57% of DON, respectively. Five strains, including *Lactococcus lactis* 6020, *Lactobacillus brevis* 1.12, *Lactobacillus casei* 6103, *Lactobacillus plantarum* 8014, and *Lactobacillus plantarum* 102, were reported to bind DON from MRS agar. Among the strains, *L. plantarum* achieved the best result (Zou et al., 2012). García et al. (2018), Juodeikiene et al. (2018), Yang, Li, Duan, and Yang (2017), and Chlebicz and Śliżewska (2019) observed the effects of DON detoxification by *Lactobacillus* sp. strains, *Pediococcus pentosaceus* strains, and metabolites *Lactobacillus rhamnosus* RC007 and *Lactobacillus plantarum* JM113.

4.2.4 | Bacteria from plants

Shi et al. (2014) screened 32 bacteria strains from peanut shells and investigated their ability to inhibit the growth of *F. graminearum* mycelia and DON production in vitro. All strains exhibited the ability to inhibit the growth of *F. graminearum*, and the suppression rate of 62.5% of them exceeded 40% after incubation for 4 days. Eighteen strains were capable of reducing the synthesis of DON by 16.69% to 90.3%. Among the strains, *B. amyloliquefaciens* strains WPS4-1 and WPP9 achieved the best results, reducing synthesis of DON by 90.3% and 88.4%, respectively. In another study, 354 bacterial strains from wheat anthers were screened, and 22 bacteria strains showed the ability to reduce DON production by 60% to 100% under green conditions. Nine strains notably reduced disease severity and DON production, and five strains decreased DON production to below the detection line. *Brevibacillus* sp. BRC263 and *Streptomyces* sp. BRC87B were identified as a potential combination of biocontrol agents (Palazzini, Ramirez, Torres, & Chulze, 2007).

4.3 | Degradation of DON by fungi

4.3.1 | Yeast

During fermentation, enzymatic activities are secreted into the food substrate or released from decomposed cells after autolysis (Karlovsky et al., 2016). Some of these activities may biotransform mycotoxins into nontoxic products (Wolf-Hall & Schwarz, 2002). Research indicates that fermentation microorganisms can adsorb mycotoxins through cell wall surface components, such as glucomannans, β-D-glucans, and mannan-oligosaccharides. Among these microorganisms, yeast exerts great potential in reducing DON, which may inhibit the growth of fungi, directly inhibit toxin production independent of the effect of growth inhibition, adsorb mycotoxins, or transform mycotoxins. Viable or nonviable probiotic yeasts and yeast cell wall products with high adsorption can reduce the bioavailability of mycotoxins. Some of these products may also be used to detoxify mycotoxins in animal husbandry.

According to Freire and Sant'Ana (2018), yeast can transform DON into D3G, 15-A-DON, and 3-ADON; however, D3G cannot be reconverted to DON. Nathanail et al. (2016) reported on the glucoside conjugation of DON by lager yeast *Saccharomyces pastorianus* A15. D3G can also be adsorbed during yeast fermentation. DON and D3G were reduced by 15% and 17%, respectively. Chlebicz and Śliżewska (2019) observed low levels of detoxifying activity in *Saccharomyces cerevisiae* yeast. DON concentration was, on average, decreased by 18.01%, 8.8%, and 33.3% after incubation for 6, 12, and 24 hr. Several findings showed that yeast reduced DON toxicity in piglets, and a study on the mechanism of action revealed that the alteration of intestinal transcriptome was reduced by *Saccharomyces cerevisiae boulardii* (Alassane-Kpembi et al., 2018). Yeast (low-fermenting yeast *Lachancea thermotolerans*) volatile organic compounds inhibited the growth of *F. graminearum* and significantly reduced DON synthesis. Reducing the availability of nutrients exerted no significant effect on the growth of *F. graminearum* but markedly decreased DON production (Zeidan, Ul-Hassan, Al-Thani, Balmas, & Jaoua, 2018). Moreover, a mixture of inorganic binders (activated carbon) and yeast cell wall contributed to DON detoxification in vitro. The highest adsorption was observed at the mixture ratio of 30:70 of 2.0% activated carbon and yeast cell wall incubated for 30, 60, and 90 min (De Souza et al., 2014). Other *Geotrichum fermentans*, *Kluyveromyces marxianus*, *Metschnikowia pulcherrima* strains and yeast cell wall products also counteract DON (Campagnollo et al., 2015; Kong, Shin, & Kim, 2014; Liu et al., 2016; Park, Parnsen, Duarte, Yiannikouris, & Kim, 2017; Patience, Myers, Ensley, Jacobs,

& Madson, 2014; Repečkienė, Levinskaitė, Paškevičius, & Raudonienė, 2013).

4.3.2 | Molds

New molds that can biotransform DON have recently been reported. The discovery of aerobic molds represents a notable development. He, Fan, Liu, and Zhang (2008) were the first to report on the isolation of an aerobic strain of *Aspergillus tubingensis* from soil and its ability to hydrolyze DON. After cultivation for 14 days, the mean degradation rate reached 94.4%. The degradation products emitted fluorescence, which was 18.1 D higher than that of DON. Garda-Buffon, Kupski, and Badiale-Furlong (2011) found that *Aspergillus oryzae* and *Rhizopus oryzae* could absorb DON in submerged fermentation as peroxidase activity increased. The highest degradation velocity occurred at the fermentation interval of 48 hr.

5 | DEGRADATION OF DON BY ENZYMES

Some enzymes or proteins produced by microorganisms can transform or conjugate mycotoxins (Paster, Menasherov, Lacey, & Fanelli, 1992; Westby, Reilly, & Bainbridge, 1997). As illustrated above, many microbes have been confirmed to detoxify DON; however, no enzymes have been thoroughly investigated (identified, purified, or characterized) to be responsible for DON biodegradation. Detoxification enzymes exhibited great potential in trichothecene management postharvest (Kabak, Dobson, & Var, 2006; Tian et al., 2016). Table 5 summarizes recent reports on enzymes and genes that have the ability to counteract DON.

DON degradation enzymes produced by bacteria were detected in cell-free filtrates and cell cultures, rather than in cell extracts, indicating that these extracellular enzymes could be purified from a bacterial culture (Shima et al., 1997). Microorganisms and enzymes detoxifying trichothecenes via hydroformylation, hydrolysis deepoxidation, hydroxylation, and glucuronidation may be prevalent in nature (He et al., 2010). Enzymes also have the advantage of substrate specialization, high efficiency, and environmental protection, which facilitate their application in mycotoxin control (Kolosova & Stroka, 2011). Use of enzymes can represent alternate DON detoxification methods. The study and application of resistance genes increase the resistance of crops to DON and contribute to the degradation. However, purifying detoxifying enzymes presents a challenge and is a time-consuming process.

5.1 | Cytochrome P450

Ito et al. (2013) reconstructed a cytochrome P450 system from the *Sphingomonas* sp. strain KSM1 in vitro and demonstrated its ability to hydroxylate DON and 3-acetyl DON. The catabolic product of DON, 16-hydroxy-DON, was used as a carbon source of *Sphingomonas* sp. strain and exerted reduced phytotoxicity to wheat.

5.2 | UDP-glycosyltransferase

Poppenberger et al. (2003) reported on a UDP-glycosyltransferase from *Arabidopsis thaliana* that can catalyze the transfer of glucose from UDP-glucose to the hydroxyl group at C3 of DON, forming 3-β-D-glucopyranosyl-4-DON. Overexpression of this enzyme led to the enhanced resistance of *Arabidopsis thaliana* to DON. 15-ADON can also be transformed. Li et al. (2015) also found that transgenic wheat expressing *HvUGT13248* (UDP-glucosyltransferase) exhibited significantly increased resistance to disease, and rapidly and efficiently transformed DON into D3G. Pasquet et al. (2016) observed that *Brachypodium distachyon* exhibited a similar enhanced resistance to DON by UDP-glycosyltransferase. These findings suggested the possible use of gene technology as a control strategy for *Fusarium* head blight and DON degradation.

5.3 | Glutathione-S-transferases

Gardiner et al. (2010) found that yeast that carried the gene-encoding cysteine biosynthetic enzyme or yeast on cysteine- or glutathione-supplemented media showed enhanced resistance to DON. The generation of DON–glutathione conjugates may reduce the toxicity of DON. The role of glutathione-S-transferases in DON detoxification was revealed in this study.

5.4 | β-Xylanases and amylolytic enzymes

Juodeikiene, Basinskiene, Vidmantiene, Makaravicius, and Bartkiene (2012) evaluated the influence of β-xylanase combined with amylolytic enzymes on DON detoxification during fermentation. Addition of β-xylanase not only increased the rate of DON detoxification but improved the quality of bioethanol as well.

5.5 | Peroxidase

Assuming that peroxidase may induce oxidation–reduction reactions when combined with DON, Feltrin et al. (2017) found that peroxidase from rice bran reduced by 20.3% of DON under optimal conditions. Garda-Buffon et al. (2011) also reported on the effect of peroxidase on DON degradation velocity in submerged fermentation.

TABLE 5 Enzymes and genes that can detoxify DON

Enzyme or gene	Degradation mechanism	Degradation product	Reference
Cytochrome P450	Hydroxylation	16-hydroxy-DON	Ito et al., 2013
UDP-glycosyltransferase	Glycosylation, enhancing the resistance of *Arabidopsis thaliana* to DON	3-β-D-glucopyranosyl-4-DON	Poppenberger et al., 2003
UDP-glycosyltransferase	Enhancing the resistance of *Brachypodium distachyon* to DON	–	Pasquet et al., 2016
HvUGT13248 expressed in wheat	Glycosylation, enhancing the resistance of wheat to DON	D3G	Li et al., 2015
Glutathione-S-transferases	Enhancing the resistance of yeast to DON	None	Gardiner et al., 2010
β-xylanases coupled with amylolytic enzyme	–	–	Juodeikiene et al., 2012
3-Acetyl DON Oxidase	Oxidation	3-keto-DON	Xu et al., 2013
Peroxidase	Oxidation–reduction reactions	Not mentioned	Feltrin et al., 2017

6 | TRENDS IN THE APPLICATION OF RNA INTERFERENCE STRATEGY, OMICS TOOLS, AND ENZYMES

Advanced technology is typically the reference for sustainable long-term strategies. Novel approaches such as genome sequencing, which can identify genes related to detoxification, need to be introduced in this field. Future strategies may also include the combination of biocontrol agents to show synergism, as suggested by Luz, Stockwell, Bergstrom, Leonard, and Bushnell (2003), who provided a number of strategies for enhancing biological control. Although many biodegradation methods have been developed, several concerns have yet to be addressed in future studies, including the following: how to reveal changes in DON and its derivatives during degradation and food processing; how to apply various degradation microorganisms or degradation enzymes during actual food production (fermentation, baking, and so on); and how to ensure the activity and safety of enzymes.

6.1 | RNA interference strategy

Apart from traditional preharvest breeding technology of disease resistance and conventional postharvest control methods, more precise biological technologies have been introduced to the preharvest control of fungal diseases and mycotoxins, including gene silencing technology and gene expression regulation mediated by designer transcription activator-like effector (Bogdanove, 2014; Koch & Kogel, 2014; Tiwari, Sharma, & Trivedi, 2014). As an efficient gene silencing technology, RNA interference can specifically eliminate or turn off the expression of specific genes, providing practical applications in agricultural treatment intervention.

RNA interference refers to the highly efficient and specific degradation of homologous mRNA mainly induced by double stranded RNA. It is the highly conserved evolutionary defense mechanism and behavior against foreign aggression, which exists universally in nearly all of eukaryotic organisms (Hannon, 2002). Both pre-transcriptional-level gene silencing and post-transcriptional-level gene silencing are included; the former is the interference of gene transcription induced by chromosomal heterochromatism or DNA methylation and so on, and the latter refers to the specific degradation of target mRNA sequence in the cytoplasm. Small interfering RNAs (siRNA) and microRNAs (miRNA), which bind with Argonaute proteins (Agos) to form RNA-induced silencing complex (RISC), are the most studied small RNAs (Khvorova, Reynolds, & Jayasena, 2003). miRNA causes translation inhibition or degradation of target gene, whereas siRNA can only lead to the degradation of target gene.

In fungi, RNA interference pathways play role in pathogenicity, genome protection, development, and antiviral defense. Most fungi conserve core RNA interference pathway components, including Dicer proteins (Dicers), RNA-dependent RNA polymerases (RdRps), and Agos. RISC formed by siRNA degrades target gene complementary to siRNA antisense chain (Gaffar, Imani, Karlovsky, Koch, & Kogel, 2019). In *F. graminearum*, endogenous genes can be blocked by hairpin RNA. Two Dicers, five RdRps, and two Agos have been identified as components involved in the silencing pathway (Chen et al., 2015). Importantly, small RNAs can be exchanged between plants and fungi. Accordingly, endogenous Host-Induced Gene Silencing (HIGS) technology and exogeneous Spray-Induced Gene Silencing (SIGS) technology have been developed to protect plants from *Fusarium* and reduce *Fusarium* mycotoxins (DON, 3-ADON,

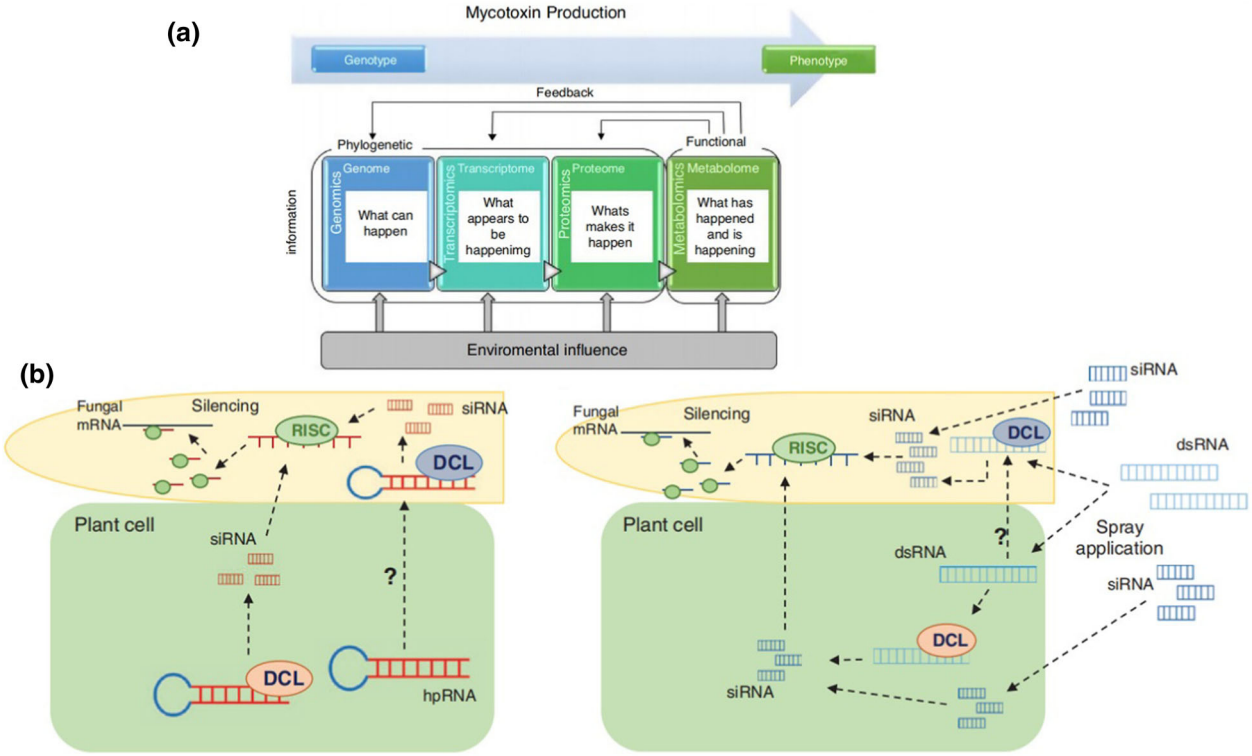

FIGURE 7 Genomic and omics technologies for mycotoxin treatment. (a) Association between mycotoxin synthesis and omics and the association between different omics (Garcia et al., 2018). (b) Possible pathways of HIGS (left) and SIGS (right) (Machado et al., 2018)
Abbreviation: DCL, Dicer-like proteins.

15-ADON, and nivalenol) contamination preharvest, as reviewed by Majumdar, Rajasekaran, and Cary (2017) and Machado, Brown, Urban, Kanyuka, and Hammond-Kosack (2018). Mediated by plant, HIGS reduce diseases in plant pathogenic fungi by silencing fungal genes in plant during attempted infection (Figure 7b). In addition, HIGS signals can be conserved to subsequent generations. On the one hand, increased disease resistance was observed in progeny seeds obtained from the initial siRNA induced seeds. On the other hand, fungal spores isolated from the original plants induced by small RNAs were still negatively affected by small RNAs signals in vitro (Majumdar et al., 2017). Table 6 summarizes published studies regarding control of DON or *Fusarium* using RNA interference technology.

RNA interference approach is a sequence-specific method and may be more specific than other techniques available for most of the grains and plants. Besides, expected gene blocking effects will not fail because of few sequence mismatching. It is expected to achieve simultaneous control of multiple plant pathogens by single silencing cassette (Machado et al., 2018). RNA interference method is conducive to greatly reducing the use of pesticides, contributing to ecosystem and human health. For instance, with its high expression of *Chs3b* on wheat ear infection, *Chs3b* was identified as the target gene for controlling *Fusarium* head blight. Silencing of *Chs3b* reduced DON significantly (van Egmond, Schothorst, & Jonker, 2007).

Challenge faced by application of RNA interference technology includes the transgenesis of HIGS, the relative short-term effectiveness of SIGS, and concerns about the possible adverse effects on humans, animals, and plants.

6.2 | Omics tools

The following conditions are generally suitable for mold growth: temperature, 10 °C to 40.5 °C, humidity, >70%; and pH, 4 to 8. Environmental factors, such as temperature, humidity, and moisture, critically affect the growth of fungi and the level of mycotoxin contamination in the food chain (Channaiah & Maier, 2014). Omics technology significantly elucidates the biological, biochemical, and biophysical molecular processes that regulate the synthesis of mycotoxins, as well as the process by which fungi adapt to diverse environmental conditions (Garcia-Cela, Verheecke-Vaessen, Magan, & Medina, 2018). The results of this study are expected to guide the investigation of more effective remedies and control strategies for mycotoxins.

Genomics, metagenomic, transcriptomics, proteomics, and metabolism are essential omics technologies and should be considered in isolation (Figure 7a). For instance,

TABLE 6 Studies regarding control of DON and *Fusarium* using HIGS and SIGS. Adapted from Majumdar et al. (2017) and Machado et al. (2018)

Host plant	Pathogen	Target gene	Method	Comments	Reference
Hordeum vulgare	*Fusarium graminearum*	*CYP51A*, *CYP51B*	HIGS	77% to 92% reduction in target gene expression, complete reduction of fungal growth with no disease symptoms in the RNAi lines	Koch et al., 2013
Barley	*Fusarium graminearum*	*CYP51A*, *CYP51B*, *CYP51C*	SIGS	Efficient inhabitation of fungal growth	Koch et al., 2016
Musa sp.	*Fusarium oxysporum* f. sp. *Cubense*	*Velvet* and *Fusarium transcription factor 1*	HIGS	7- to 25-fold reduction in conidiophores count, increased resistance (70% to 85%) to *Fusarium* wilt	Ghag, Shekhawat, & Ganapathi, 2014
Triticum aestivum L.	*Fusarium graminearum*	*Chs3b*	HIGS	1.4- to 4-fold reduction in Chs 3b expression; 78% to 85% reduction in DON	Cheng et al., 2015
Arabidopsis thaliana	*Fusarium oxysporum*	F-box protein required for pathogenicity 1, *F. oxysporum* wilt 2, 12-oxophytodienoate-10, 11-*reductase* gene	HIGS	60% to 90% reduction in target genes expression; 15% to 60% increase in plant survival, significantly lesser number of yellow leaves	Hu, Parekh, Maruta, Trusov, & Botella, 2015
Triticum aestivum	*Fusarium culmorum*	β-1,3-glucan synthase	HIGS	Several fold reduction to complete silencing of *FcGls 1* expression; 50% to 60% reduction in disease symptoms	Chen et al., 2016

genome-wide association studies (Gas) is a new powerful strategy to find novel genes related to quantitative traits. Single nucleotide polymorphisms are employed as molecular genetic markers for correlation and comparative analysis to identify genetic variation affecting complex traits. Using 119 *F. graminearum* strains from different environments, 29 quantitative trait nucleotides related with the synthesis of DON were identified by Gas (Talas, Kalih, Miedaner, & McDonald, 2016). At present, genome sequencing study is used in is not only widely used for analysis of fungi producing mycotoxins, but also used for analysis of organisms degrading mycotoxins or inhibiting the producing of mycotoxins. Moreover, bioinformation of sequencing can be used to explore potential metabolites in genome. Metabolites are the expression results of gene and proteins, and should be understood combined with stress at molecular and transcriptome level (Garcia-Cela et al., 2018). Palazzini, Dunlap, Bowman, and Chulze (2016) isolated a *Bacillus subtilis* protecting plants against *Fusarium*, and identified the taxonomy and 10 secondary metabolites of the strain by employing phylogenomic strategy. Another idea is that future studies of transcriptional data and temporal macro genome in three-dimensional environmental interactions of stress factors can provide breakthrough information to explain fungal interactions and the dominance of varying fungal communities. Consequently, beneficial microorganisms for biological control in a given ecosystem will be identified (Garcia-Cela et al., 2018).

6.3 | Enzymes

Detoxification enzymes may potentially eliminate DON in foods or feeds. Compared with microorganisms, enzyme degradation is safer without pollution risk and healthy risk, and has better repeatability and uniformity. Enzymes may be used either in free form or in immobilized form, and can be combined with industrial production, such as fermentation, to form fixed food production processes, which show a wide range of application prospects in food industry. For feed, enzymes can also be used as feed additives to degrade mycotoxins (Loi, Fanelli, Liuzzi, Logrieco, & Mulè, 2017). Enzymes coupled with the gene method provide new ideals for DON detoxification. Detoxification genes such as UDP-glucosyltransferase may be cloned and expressed in crops or microorganisms to produce resistance or massive and economical productions. Several reports have identified several detoxification genes and demonstrated their contributory effects on DON degradation.

On the basis of the aforementioned microorganism, we assumed that some active enzymes may be responsible for the degradation of DON. The enzymes specifically exert a degradation effect on DON, which can destroy the DON structure,

producing nontoxic or toxic products, as shown in Table 5. The degradation mechanism and degradation products have yet to be determined. Purification, characterization, and the harsh operating conditions of enzymes may elucidate their application in DON detoxification. The challenge in the successful application of enzymes in food production lies in the low yield, complex purification and production processes, instability of properties, and harsh conditions of the enzymes. The safety of the degradation products and impact on food or feed should also be considered.

7 | CONCLUSION

Studies on the biological removal of DON have been conducted both in vivo and in vitro. Increased attention has recently been paid to the identification, transformation action, and toxicologic study of already known or unknown modified forms of DON during food processing and biological degradation. An in-depth investigation into the metabolism, toxicologic evaluation, risk assessment, and detoxification mechanism of known and unknown degradation products is desirable. New mechanisms for mitigating DON have also been revealed. Published articles and patents indicate that the use of both microorganisms and enzymes to decontaminate food commodities draws interest. The emergence of commercialized degradation biological/enzymatic agents emphasizes the potential of this approach. The advantages include (a) specificity of the reaction; (b) mildness of the reaction, particularly for pH and temperature; (c) reduced impact on food quality; (d) applicability and feasibility in the foodstuff industry; (e) environmental conservation; and (f) application potential of the enzymes.

DON can be reduced significantly during food processing owing to its binding ability to food matrix, transformation, dilution, or mitigation. Enzymes and additives used during food processing, which induce a decrease in DON reduction, should be paid special attention. D3G, 3-ADON, and DOM-1 have been found to increase during bread making and baby food production. Thermal degradation products, including isoDON, DOM1, norDON A, norDON B, norDON C, norDON D, norDON E, norDON F, and hy-DON-lac, have been identified. DON, modified DON, and thermal degradation products need to be monitored during food production.

Degrading microorganism and enzymes exhibit potential for application in food production and may present a challenge. Currently, the use of enzymes for DON degradation in practical production is rarely reported. Novel techniques, such as RNA interference and omics, improve our understanding of mycotoxins and would be useful in the investigation of more effective mycotoxin treatment strategies. Undesirable situations for degradation have been noted. Only one strain has thus far been authorized for feed additives, and no microbial enzyme has been officially authorized as a processing aid for DON detoxification in food. Numerous challenges have yet to be overcome for the successful commercial application of microorganisms. Challenges may include insights into degradation mechanisms, identification of effective elimination in food/feed substrate, stability and suitability of detoxification agents, safety of degradation products, and successful application for industrial production. All of these would require regulatory approval.

AUTHOR CONTRIBUTIONS

Hongyan Guo collected the references and wrote the majority of the manuscript. Jian Ji wrote the structure analysis part and drew the molecular structure diagram of DON and modified forms. Professor Xiulan Sun and Jia-sheng Wang reviewed the manuscript. Professor Xiulan Sun approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (No. 31772069), National First-class Discipline Program of Food Science and Technology (No. JUFSTR 20180303), and Synergistic Innovation Center of Food Safety and Nutrition.

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REFERENCES

Ahad, R., Zhou, T., Lepp, D., & Pauls, K. P. (2017). Microbial detoxification of eleven food and feed contaminating trichothecene mycotoxins. *BMC Biotechnology*, *17*(1), 30. https://doi.org/10.1186/s12896-017-0352-7

Ajandouz, E., Berdah, S., Moutardier, V., Bege, T., Birnbaum, D., Perrier, J., … Maresca, M. (2016). Hydrolytic fate of 3/15-acetyldeoxynivalenol in humans: Specific deacetylation by the small intestine and liver revealed using in vitro and ex vivo approaches. *Toxins*, *8*(8), 232. https://doi.org/10.3390/toxins8080232

Alassane-Kpembi, I., Pinton, P., Hupé, J.-F., Neves, M., Lippi, Y., Combes, S., … Oswald, I. (2018). Saccharomyces cerevisiae boulardii reduces the deoxynivalenol-induced alteration of the intestinal transcriptome. *Toxins*, *10*(5), 199. https://doi.org/10.3390/toxins10050199

Alassane-Kpembi, I., Puel, O., & Oswald, I. P. (2015). Toxicological interactions between the mycotoxins deoxynivalenol, nivalenol and their acetylated derivatives in intestinal epithelial cells. *Archives of Toxicology*, *89*(8), 1337–1346. https://doi.org/10.1007/s00204-014-1309-4

Awad, W. A., Ghareeb, K., Böhm, J., & Zentek, J. (2010). Decontamination and detoxification strategies for the *Fusarium* mycotoxin deoxynivalenol in animal feed and the effectiveness of microbial biodegradation. *Food Additives & Contaminants*, *27*(4), 510–520. https://doi.org/10.1080/19440040903571747

Bennett, J. W., & Klich, M. (2003). Mycotoxins. *Clinical Microbiology Reviews*, *16*(3), 497–516. https://doi.org/10.1128/CMR.16.3.497-516.2003

Bergamini, E., Catellani, D., Dall'Asta, C., Galaverna, G., Dossena, A., Marchelli, R., & Suman, M. (2010). Fate of *Fusarium* mycotoxins in the cereal product supply chain: The deoxynivalenol (DON) case within industrial bread-making technology. *Food Additives & Contaminants*, *27*(5), 677–687. https://doi.org/10.1080/19440041003660117

Berthiller, F., Crews, C., Dall'Asta, C., Saeger, S. D., Haesaert, G., Karlovsky, P., … Stroka, J. (2013). Masked mycotoxins: A review. *Molecular Nutrition & Food research*, *57*(1), 165–186. https://doi.org/10.1002/mnfr.201100764

Berthiller, F., Dall'Asta, C., Corradini, R., Marchelli, R., Sulyok, M., Krska, R., … Schuhmacher, R. (2009). Occurrence of deoxynivalenol and its 3-β-D-glucoside in wheat and maize. *Food Additives & Contaminants*, *26*(4), 507–511. https://doi.org/10.1080/02652030802555668

Berthiller, F., Krska, R., Domig, K. J., Kneifel, W., Juge, N., Schuhmacher, R., & Adam, G. (2011). Hydrolytic fate of deoxynivalenol-3-glucoside during digestion. *Toxicology Letters*, *206*(3), 264–267. https://doi.org/10.1016/j.toxlet.2011.08.006

Binder, J., Horvath, E., Schatzmayr, G., Ellend, N., Danner, H., Krska, R., & Braun, R. (1997). Screening for deoxynivalenol-detoxifying anaerobic rumen microorganisms. *Cereal Research Communications*, *25*, 343–346.

Biomin (2019). *Biomin world mycotoxin survey report 2018*. Retrieved from https://www.biomin.net/nz/articles/biomin-world-mycotoxin-survey-report-2018/

Blanca, E., Guevara, Y., & Yoshizawa, T. (2004). Heat-induced isomers of acetylated derivatives of deoxynivalenol and nivalenol. *JSM Mycotoxins*, *2003*(Suppl 3), 337–343. https://doi.org/10.2520/myco1975.2003.Suppl3_337

Bogdanove, A. J. (2014). Principles and applications of TAL effectors for plant physiology and metabolism. *Current Opinion in Plant Biology*, *19*, 99–104. https://doi.org/10.1016/j.pbi.2014.05.007

Boyacioğlu, D., Heltiarachchy, N. S., & d'appolonia, B. L. (1993). Additives affect deoxynivalenol (vomi toxin) flour during breadbaking. *Journal of Food Science*, *58*(2), 416–418.

Bretz, M., Beyer, M., Cramer, B., Knecht, A., & Humpf, H.-U. (2006). Thermal degradation of the *Fusarium* mycotoxin deoxynivalenol. *Journal of Agricultural and Food Chemistry*, *54*(17), 6445–6451. https://doi.org/10.1021/jf061008g

Brodehl, A., Möller, A., Kunte, H.-J., Koch, M., & Maul, R. (2014). Biotransformation of the mycotoxin zearalenone by fungi of the genera *Rhizopus* and *Aspergillus*. *FEMS Microbiology Letters*, *359*(1), 124–130. https://doi.org/10.1111/1574-6968.12586

Broekaert, N., Devreese, M., De Baere, S., De Backer, P., & Croubels, S. (2015). Modified *Fusarium* mycotoxins unmasked: From occurrence in cereals to animal and human excretion. *Food and Chemical Toxicology*, *80*, 17–31. https://doi.org/10.1016/j.fct.2015.02.015

Broekaert, N., Devreese, M., De Mil, T., Fraeyman, S., Antonissen, G., De Baere, S., … Croubels, S. (2015). Oral bioavailability, hydrolysis, and comparative toxicokinetics of 3-acetyldeoxynivalenol and 15-acetyldeoxynivalenol in broiler chickens and pigs. *Journal of Agricultural and Food Chemistry*, *63*(39), 8734–8742. https://doi.org/10.1021/acs.jafc.5b03270

Broekaert, N., Devreese, M., Demeyere, K., Berthiller, F., Michlmayr, H., Varga, E., … Croubels, S. (2016). Comparative in vitro cytotoxicity of modified deoxynivalenol on porcine intestinal epithelial cells. *Food and Chemical Toxicology*, *95*, 103–109. https://doi.org/10.1016/j.fct.2016.06.012

Bullerman, L. B., Giesova, M., Hassan, Y., Deibert, D., & Ryu, D. (2006). Antifungal activity of sourdough bread cultures. In A. D. Hocking, J. I. Pitt, R. A. Samson, & U. Thrane (Eds.), *Advances in food mycology* (Vol. *571*, pp. 307–316). Boston, MA: Springer. https://doi.org/10.1007/0-387-28391-9_20

Campagnollo, F. B., Franco, L. T., Rottinghaus, G. E., Kobashigawa, E., Ledoux, D. R., Daković, A., & Oliveira, C. A. (2015). In vitro evaluation of the ability of beer fermentation residue containing *Saccharomyces cerevisiae* to bind mycotoxins. *Food Research International*, *77*, 643–648. https://doi.org/10.1016/j.foodres.2015.08.032

Cano-Sancho, G., Gauchi, J.-P., Sanchis, V., Marín, S., & Ramos, A. J. (2011). Quantitative dietary exposure assessment of the Catalonian population (Spain) to the mycotoxin deoxynivalenol. *Food Additives & Contaminants: Part A*, *28*(8), 1098–1109. https://doi.org/10.1080/19440049.2011.576445

Cano-Sancho, G., Sanchis, V., Ramos, A. J., & Marín, S. (2013). Effect of food processing on exposure assessment studies with mycotoxins. *Food Additives & Contaminants: Part A*, *30*(5), 867–875. https://doi.org/10.1080/19440049.2013.793824

Carere, J., Hassan, Y. I., Lepp, D., & Zhou, T. (2018). The enzymatic detoxification of the mycotoxin deoxynivalenol: Identification of DepA from the DON epimerization pathway. *Microbial Biotechnology*, *11*(6), 1106–1111. https://doi.org/10.1111/1751-7915.12874

Channaiah, L. H., & Maier, D. E. (2014). Best stored maize management practices for the prevention of mycotoxin contamination. In J. F. Leslie & A. F. Logrieco (Eds.), *Mycotoxin reduction in grain chains* (pp. 78–87). Chichester, UK: John Wiley & Sons. https://doi.org/10.1002/9781118832790.ch6

Cheli, F., Pinotti, L., Rossi, L., & Dell'Orto, V. (2013). Effect of milling procedures on mycotoxin distribution in wheat fractions: A review. *LWT—Food Science and Technology*, *54*(2), 307–314. https://doi.org/10.1016/j.lwt.2013.05.040

Chen, W., Kastner, C., Nowara, D., Oliveira-Garcia, E., Rutten, T., Zhao, Y., … Schweizer, P. (2016). Host-induced silencing of *Fusarium* culmorum genes protects wheat from infection. *Journal of Experimental Botany*, *67*(17), 4979–4991. https://doi.org/10.1093/jxb/erw263

Chen, Y., Gao, Q., Huang, M., Liu, Y., Liu, Z., Liu, X., & Ma, Z. (2015). Characterization of RNA silencing components in the plant pathogenic fungus *Fusarium graminearum*. *Scientific Reports*, *5*, 12500. https://doi.org/10.1038/srep12500

Cheng, W., Song, X. S., Li, H. P., Cao, L. H., Sun, K., Qiu, X. L., … Qu, B. (2015). Host-induced gene silencing of an essential chitin synthase gene confers durable resistance to *Fusarium* head blight and seedling blight in wheat. *Plant Biotechnology Journal*, *13*(9), 1335–1345. https://doi.org/10.1111/pbi.12352

Chilaka, C. A., De Boevre, M., Atanda, O. O., & De Saeger, S. (2019). Fate of *Fusarium* mycotoxins during processing of Nigerian traditional infant foods (ogi and soybean powder). *Food Research International*, *116*, 408–418. https://doi.org/10.1016/j.foodres.2018.08.055

Chlebicz, A., & Śliżewska, K. (2019). In vitro detoxification of aflatoxin B 1, deoxynivalenol, fumonisins, T-2 Toxin and

zearalenone by probiotic bacteria from genus lactobacillus and saccharomyces cerevisiae yeast. *Probiotics and Antimicrobial Proteins*. https://doi.org/10.1007/s12602-018-9512-x

Cote, L. M., Nicoletti, J., Swanson, S. P., & Buck, W. B. (1986). Production of deepoxydeoxynivalenol (DOM-1), a metabolite of deoxynivalenol, by in vitro rumen incubation. *Journal of Agricultural and Food Chemistry*, *34*(3), 458–460. https://doi.org/10.1021/jf00069a020

Côté, L.-M., Dahlem, A., Yoshizawa, T., Swanson, S., & Buck, W. (1986). Excretion of deoxynivalenol and its metabolite in milk, urine, and feces of lactating dairy cows. *Journal of Dairy Science*, *69*(9), 2416–2423. https://doi.org/10.3168/jds.S0022-0302(86)80681-6

Daenicke, S., Keese, C., Goyarts, T., & Döll, S. (2011). Effects of deoxynivalenol (DON) and related compounds on bovine peripheral blood mononuclear cells (PBMC) in vitro and in vivo. *Mycotoxin Research*, *27*(1), 49–55. https://doi.org/10.1007/s12550-010-0074-3

Dalié, D., Deschamps, A., & Richard-Forget, F. (2010). Lactic acid bacteria—Potential for control of mould growth and mycotoxins: A review. *Food Control*, *21*(4), 370–380. https://doi.org/10.1016/j.foodcont.2009.07.011

Dänicke, S., Hegewald, A. -K., Kahlert, S., Kluess, J., Rothkötter, H.-J., Breves, G., & Döll, S. (2010). Studies on the toxicity of deoxynivalenol (DON), sodium metabisulfite, DON-sulfonate (DONS) and de-epoxy-DON for porcine peripheral blood mononuclear cells and the Intestinal Porcine Epithelial Cell lines IPEC-1 and IPEC-J2, and on effects of DON and DONS on piglets. *Food and Chemical Toxicology*, *48*, 8–9. https://doi.org/10.1016/j.fct.2010.05.022

De Souza, A., Borsato, D., Lofrano, A., De Oliveira, A., Ono, M., Bordini, J., … Ono, E. (2014). In vitro removal of deoxynivalenol by a mixture of organic and inorganic adsorbents. *World Mycotoxin Journal*, *8*(1), 113–119. https://doi.org/10.3920/WMJ2013.1666

Dinu, D., Bodea, G. O., Ceapa, C. D., Munteanu, M. C., Roming, F. I., Serban, A. I., … Dinischiotu, A. (2011). Adapted response of the antioxidant defense system to oxidative stress induced by deoxynivalenol in Hek-293 cells. *Toxicon*, *57*(7-8), 1023–1032. https://doi.org/1023-1032.10.1016/j.toxicon.2011.04.006

Edwards, S. G., Dickin, E., Macdonald, S., Buttler, D., Hazel, C., Patel, S., & Scudamore, K. (2011). Distribution of *Fusarium* mycotoxins in UK wheat mill fractions. *Food Additives & Contaminants: Part A*, *28*(12), 1694–1704. https://doi.org/10.1080/19440049.2011.605770

Eriksen, G. S., Pettersson, H., & Lindberg, J. (2003). Absorption, metabolism and excretion of 3-acetyl DON in pigs. *Archives of Animal Nutrition*, *57*(5), 335–345. https://doi.org/10.1080/00039420310001607699

Eriksen, G. S., Pettersson, H., & Lundh, T. (2004). Comparative cytotoxicity of deoxynivalenol, nivalenol, their acetylated derivatives and de-epoxy metabolites. *Food and Chemical Toxicology*, *42*(4), 619–624. https://doi.org/10.1016/j.fct.2003.11.006

European Food Safety Authority (EFSA). (2005). Opinion of the scientific panel on additives and products or substances used in animal feed (FEEDAP) on the safety of the product "Biomin BBSH 797" for piglets, pigs for fattening and chickens for fattening. *EFSA Journal*, *3*(2). 169.

FAO/WHO. (2002). *Guidelines for the evaluation of probiotics in food*. Geneva, Switzerland: WHO.

Feltrin, A. C. P., Garcia, S. D. O., Caldas, S. S., Primel, E. G., Badiale-Furlong, E., & Garda-Buffon, J. (2017). Characterization and application of the enzyme peroxidase to the degradation of the mycotoxin DON. *Journal of Environmental Science and Health, Part B*, *52*(10), 777–783. https://doi.org/10.1080/03601234.2017.1356672

Franco, T. S., Garcia, S., Hirooka, E. Y., Ono, Y. S., & dos Santos, J. S. (2011). Lactic acid bacteria in the inhibition of *Fusarium graminearum* and deoxynivalenol detoxification. *Journal of Applied Microbiology*, *111*(3), 739–748. https://doi.org/10.1111/j.1365-2672.2011.05074.x

Freire, L., & Sant'Ana, A. S. (2018). Modified mycotoxins: An updated review on their formation, detection, occurrence, and toxic effects. *Food and Chemical Toxicology*, *111*, 189–205. https://doi.org/10.1016/j.fct.2017.11.021

Fuchs, E., Binder, E., Heidler, D., & Krska, R. (2002). Structural characterization of metabolites after the microbial degradation of type A trichothecenes by the bacterial strain BBSH 797. *Food Additives & Contaminants*, *19*(4), 379–386. https://doi.org/10.1080/02652030110091154

Gaffar, F. Y., Imani, J., Karlovsky, P., Koch, A., & Kogel, K. H. (2019). Different components of the RNA interference machinery are required for conidiation, ascosporogenesis, virulence, deoxynivalenol production, and fungal inhibition by exogenous double-stranded RNA in the head blight pathogen *Fusarium graminearum*. *Frontiers in Microbiology*, *10*, 1662–1662. https://doi.org/10.3389/fmicb.2019.01662

Gao, X., Mu, P., Wen, J., Sun, Y., Chen, Q., & Deng, Y. (2018). Detoxification of trichothecene mycotoxins by a novel bacterium, Eggerthella sp. DII-9. *Food and Chemical Toxicology*, *112*, 310–319. https://doi.org/10.1016/j.fct.2017.12.066

García, G. R., Payros, D., Pinton, P., Dogi, C. A., Laffitte, J., Neves, M., … Oswald, I. P. (2018). Intestinal toxicity of deoxynivalenol is limited by Lactobacillus rhamnosus RC007 in pig jejunum explants. *Archives of Toxicology*, *92*(2), 983–993. https://doi.org/10.1007/s00204-017-2083-x

Garcia-Cela, E., Verheecke-Vaessen, C., Magan, N., & Medina, A. (2018). The "-omics" contributions to the understanding of mycotoxin production under diverse environmental conditions. *Current Opinion in Food Science*, *23*, 97–104. https://doi.org/10.1016/j.cofs.2018.08.005

Garda-Buffon, J., Kupski, L., & Badiale-Furlong, E. (2011). Deoxynivalenol (DON) degradation and peroxidase enzyme activity in submerged fermentation. *Food Science and Technology*, *31*(1), 198–203. https://doi.org/10.1590/s0101-20612011000100030

Gardiner, S. A., Boddu, J., Berthiller, F., Hametner, C., Stupar, R. M., Adam, G., & Muehlbauer, G. J. (2010). Transcriptome analysis of the barley–deoxynivalenol interaction: Evidence for a role of glutathione in deoxynivalenol detoxification. *Molecular Plant-Microbe Interactions*, *23*(7), 962–976. https://doi.org/10.1094/mpmi-23-7-0962

Gärtner, B. H., Munich, M., Kleijer, G., & Mascher, F. (2008). Characterisation of kernel resistance against *Fusarium* infection in spring wheat by baking quality and mycotoxin assessments. *European Journal of Plant Pathology*, *120*(1), 61–68. https://doi.org/10.1007/s10658-007-9198-5

Generotti, S., Cirlini, M., Malachova, A., Sulyok, M., Berthiller, F., Dall'Asta, C., & Suman, M. (2015). Deoxynivalenol & deoxynivalenol-3-glucoside mitigation through bakery production strategies: Effective experimental design within industrial rusk-making technology. *Toxins*, *7*(8), 2773–2790. https://doi.org/10.3390/toxins7082773

Generotti, S., Cirlini, M., Šarkanj, B., Sulyok, M., Berthiller, F., Dall'Asta, C., & Suman, M. (2017). Formulation and processing factors affecting trichothecene mycotoxins within industrial biscuit-making. *Food Chemistry*, *229*, 597–603. https://doi.org/10.1016/j.foodchem.2017.02.115

Ghag, S. B., Shekhawat, U. K., & Ganapathi, T. R. (2014). Host-induced post-transcriptional hairpin RNA-mediated gene silencing of vital fungal genes confers efficient resistance against *Fusarium* wilt in banana. *Plant Biotechnology Journal*, *12*(5), 541–553. https://doi.org/10.1111/pbi.12158

Gourama, H., & Bullerman, L. B. (1995). Antimycotic and anti-aflatoxigenic effect of lactic acid bacteria: A review. *Journal of Food Protection*, *58*(11), 1275–1280. https://doi.org/10.4315/0362-028x-58.11.1275

Gratz, S. W., Duncan, G., & Richardson, A. J. (2013). The human fecal microbiota metabolizes deoxynivalenol and deoxynivalenol-3-glucoside and may be responsible for urinary deepoxy-deoxynivalenol. *Applied and Environmental Microbiology*, *79*(6), 1821–1825. https://doi.org/10.1128/AEM.02987-12

Grenier, B., Bracarense, A.-P. F., Schwartz, H. E., Lucioli, J., Cossalter, A.-M., Moll, W.-D., … Oswald, I. P. (2013). Biotransformation approaches to alleviate the effects induced by *Fusarium* mycotoxins in swine. *Journal of Agricultural and Food Chemistry*, *61*(27), 6711–6719. https://doi.org/10.1021/jf400213q

Guan, S., He, J., Young, J. C., Zhu, H., Li, X.-Z., Ji, C., & Zhou, T. (2009). Transformation of trichothecene mycotoxins by microorganisms from fish digesta. *Aquaculture*, *290*(3–4), 290–295. https://doi.org/10.1016/j.aquaculture.2009.02.037

Guerrero-Netro, H. M., Estienne, A., Chorfi, Y., & Price, C. A. (2017). The mycotoxin metabolite deepoxy-deoxynivalenol increases apoptosis and decreases steroidogenesis in bovine ovarian theca cells. *Biology of Reproduction*, *97*(5), 746–757. https://doi.org/10.1093/biolre/iox127

Hannon, G. J. (2002). RNA interference. *Nature*, *418*(6894), 244–251. https://doi.org/10.1038/418244a

Haskard, C. A., El-Nezami, H. S., Kankaanpää, P. E., Salminen, S., & Ahokas, J. T. (2001). Surface binding of aflatoxin B1 by lactic acid bacteria. *Applied and Environmental Microbiology*, *67*(7), 3086–3091. https://doi.org/10.1128/aem.67.7.3086-3091.2001

Hassan, Y. I., & Bullerman, L. B. (2013). Cell-surface binding of deoxynivalenol to *Lactobacillus paracasei* subsp. tolerans isolated from sourdough starter culture. *The Journal of Microbiology, Biotechnology and Food Sciences*, *2*(5), 2323.

Hassan, Y. I., He, J. W., Perilla, N., Tang, K., Karlovsky, P., & Zhou, T. (2017). The enzymatic epimerization of deoxynivalenol by Devosia mutans proceeds through the formation of 3-keto-DON intermediate. *Scientific Reports*, *7*(1), 6929. https://doi.org/10.1038/s41598-017-07319-0

Hathout, A. S., & Aly, S. E. (2014). Biological detoxification of mycotoxins: A review. *Annals of Microbiology*, *64*(3), 905–919. https://doi.org/10.1007/s13213-014-0899-7

He, C., Fan, Y., Liu, G., & Zhang, H. (2008). Isolation and identification of a strain of *Aspergillus tubingensis* with deoxynivalenol biotransformation capability. *International Journal of Molecular Sciences*, *9*(12), 2366–2375. https://doi.org/10.3390/ijms9122366

He, J. W., Bondy, G. S., Zhou, T., Caldwell, D., Boland, G. J., & Scott, P. M. (2015). Toxicology of 3-epi-deoxynivalenol, a deoxynivalenol-transformation product by Devosia mutans 17-2-E-8. *Food and Chemical Toxicology*, *84*, 250–259. https://doi.org/10.1016/j.fct.2015.09.003

He, J. W., Hassan, Y. I., Perilla, N., Li, X.-Z., Boland, G. J., & Zhou, T. (2016). Bacterial epimerization as a route for deoxynivalenol detoxification: The influence of growth and environmental conditions. *Frontiers in Microbiology*, *7*, 572. https://doi.org/10.3389/fmicb.2016.00572

He, J., Boland, G., & Zhou, T. (2009). Concurrent selection for microbial suppression of *Fusarium graminearum*, *Fusarium* head blight and deoxynivalenol in wheat. *Journal of Applied Microbiology*, *106*(6), 1805–1817. https://doi.org/10.1111/j.1365-2672.2009.04147.x

He, J., Zhou, T., Young, J. C., Boland, G. J., & Scott, P. M. (2010). Chemical and biological transformations for detoxification of trichothecene mycotoxins in human and animal food chains: A review. *Trends in Food Science & Technology*, *21*(2), 67–76. https://doi.org/10.1016/j.tifs.2009.08.002

He, P., Young, L., & Forsberg, C. (1992). Microbial transformation of deoxynivalenol (vomitoxin). *Applied and Environmental Microbiology*, *58*(12), 3857–3863. https://doi.org/10.1002/bit.260401020

Hocking, A. D., Pitt, J. I., Samson, R. A., & Thrane, U. (2006). *Advances in food mycology*. Boston, MA: Springer. https://doi.org/10.1111/j.1365-2621.2006.01205.x

Hu, Z., Parekh, U., Maruta, N., Trusov, Y., & Botella, J. R. (2015). Down-regulation of *Fusarium* oxysporum endogenous genes by host-delivered RNA interference enhances disease resistance. *Frontiers in Chemistry*, *3*, 1. https://doi.org/10.3389/fchem.2015.00001

Hussain, S. S., & Bloom, S. R. (2013). The regulation of food intake by the gut-brain axis: Implications for obesity. *International journal of obesity*, *37*(5), 625–633. https://doi.org/10.1038/ijo.2012.93

Ikunaga, Y., Sato, I., Grond, S., Numaziri, N., Yoshida, S., Yamaya, H., … Koitabashi, M. (2011). Nocardioides sp. strain WSN05-2, isolated from a wheat field, degrades deoxynivalenol, producing the novel intermediate 3-epi-deoxynivalenol. *Applied Microbiology and Biotechnology*, *89*(2), 419–427. https://doi.org/10.1007/s00253-010-2857-z

Indira, K., Jayalakshmi, S., Gopalakrishnan, A., & Srinivasan, M. (2011). Biopreservative potential of marine *Lactobacillus* spp. *African Journal of Microbiology Research*, *5*(16), 2287–2296.

Ito, M., Sato, I., Ishizaka, M., Yoshida, S.-i., Koitabashi, M., Yoshida, S., & Tsushima, S. (2013). Bacterial cytochrome P450 system catabolizing the *Fusarium* toxin deoxynivalenol. *Applied and Environmental Microbiology*, *79*(5), 1619–1628. https://doi.org/10.1128/aem.03227-12

Ito, M., Sato, I., Koitabashi, M., Yoshida, S., Imai, M., & Tsushima, S. (2012). A novel actinomycete derived from wheat heads degrades deoxynivalenol in the grain of wheat and barley affected by *Fusarium* head blight. *Applied Microbiology and Biotechnology*, *96*(4), 1059–1070. https://doi.org/10.1007/s00253-012-3922-6

Ivanova, L., Sahlstrøm, S., Rud, I., Uhlig, S., Fæste, C. K., Eriksen, G. S., & Divon, H. H. (2017). Effect of primary processing on the distribution of free and modified *Fusarium* mycotoxins in naturally contaminated oats. *World Mycotoxin Journal*, *10*(1), 73–88. https://doi.org/10.3920/WMJ2016.2092

Juan, C., Raiola, A., Mañes, J., & Ritieni, A. (2014). Presence of mycotoxin in commercial infant formulas and baby foods from Italian market. *Food Control*, *39*, 227–236. https://doi.org/10.1016/j.foodcont.2013.10.036

Juan-García, A., Juan, C., Tolosa, J., & Ruiz, M.-J. (2019). Effects of deoxynivalenol, 3-acetyl-deoxynivalenol and 15-acetyl-deoxynivalenol on parameters associated with oxidative stress in HepG2 cells. *Mycotoxin Research*, *35*(2), 197–205. https://doi.org/10.1007/s12550-019-00344-0

Juan-García, A., Taroncher, M., Font, G., & Ruiz, M.-J. (2018). Micronucleus induction and cell cycle alterations produced by deoxynivalenol and its acetylated derivatives in individual and combined exposure on HepG2 cells. *Food and Chemical Toxicology*, *118*, 719–725. https://doi.org/10.1016/j.fct.2018.06.024

Juodeikiene, G., Bartkiene, E., Cernauskas, D., Cizeikiene, D., Zadeike, D., Lele, V., & Bartkevics, V. (2018). Antifungal activity of lactic acid bacteria and their application for *Fusarium* mycotoxin reduction in malting wheat grains. *LWT—Food Science and Technology*, *89*, 307–314. https://doi.org/10.1016/j.lwt.2017.10.061

Juodeikiene, G., Basinskiene, L., Vidmantiene, D., Makaravicius, T., & Bartkiene, E. (2012). Benefits of β-xylanase for wheat biomass conversion to bioethanol. *Journal of the Science of Food and Agriculture*, *92*(1), 84–91. https://doi.org/10.1002/jsfa.4545

Kabak, B., Dobson, A. D., & Var, I. l. (2006). Strategies to prevent mycotoxin contamination of food and animal feed: A review. *Critical Reviews in Food Science and Nutrition*, *46*(8), 593–619. https://doi.org/10.1080/10408390500436185

Kadota, T., Furusawa, H., Hirano, S., Tajima, O., Kamata, Y., & Sugita-Konishi, Y. (2013). Comparative study of deoxynivalenol, 3-acetyldeoxynivalenol, and 15-acetyldeoxynivalenol on intestinal transport and IL-8 secretion in the human cell line Caco-2. *Toxicology in Vitro*, *27*(6), 1888–1895. https://doi.org/10.1016/j.tiv.2013.06.003

Karlovsky, P. (2011). Biological detoxification of the mycotoxin deoxynivalenol and its use in genetically engineered crops and feed additives. *Applied Microbiology and Biotechnology*, *91*(3), 491–504. https://doi.org/10.1007/s00253-011-3401-5

Karlovsky, P., Suman, M., Berthiller, F., De Meester, J., Eisenbrand, G., Perrin, I., … Recker, T. (2016). Impact of food processing and detoxification treatments on mycotoxin contamination. *Mycotoxin Research*, *32*(4), 179–205. https://doi.org/10.1007/s12550-016-0257-7

Khaneghah, A. M., Martins, L. M., von Hertwig, A. M., Bertoldo, R., & Sant'Ana, A. S. (2018). Deoxynivalenol and its masked forms: Characteristics, incidence, control and fate during wheat and wheat based products processing—A review. *Trends in Food Science & Technology*, *71*, 13–24. https://doi.org/10.1016/j.tifs.2017.10.012

Khatibi, P. A., Berger, G., Wilson, J., Brooks, W. S., McMaster, N., Griffey, C. A., … Schmale, D. G., III. (2014). A comparison of two milling strategies to reduce the mycotoxin deoxynivalenol in barley. *Journal of Agricultural and Food Chemistry*, *62*(18), 4204–4213. https://doi.org/10.1021/jf501208x

Khvorova, A., Reynolds, A., & Jayasena, S. D. (2003). Functional siRNAs and miRNAs exhibit strand bias. *Cell*, *115*(2), 209–216. https://doi.org/10.1016/S0092-8674(03)00801-8

King, R. R., McQueen, R. E., Levesque, D., & Greenhalgh, R. (1984). Transformation of deoxynivalenol (vomitoxin) by rumen microorganisms. *Journal of Agricultural and Food Chemistry*, *32*(5), 1181–1183. https://doi.org/10.1021/jf00125a061

Koch, A., Biedenkopf, D., Furch, A., Weber, L., Rossbach, O., Abdellatef, E., … Cardoza, V. (2016). An RNAi-based control of *Fusarium graminearum* infections through spraying of long dsRNAs involves a plant passage and is controlled by the fungal silencing machinery. *PLoS Pathogens*, *12*(10), e1005901. https://doi.org/10.1371/journal.ppat.1005901

Koch, A., & Kogel, K. H. (2014). New wind in the sails: Improving the agronomic value of crop plants through RNA i-mediated gene silencing. *Plant Biotechnology Journal*, *12*(7), 821–831. https://doi.org/10.1111/pbi.12226

Koch, A., Kumar, N., Weber, L., Keller, H., Imani, J., & Kogel, K. H. (2013). Host-induced gene silencing of cytochrome P450 lanosterol C14α-demethylase–encoding genes confers strong resistance to *Fusarium* species. *Proceedings of the National Academy of Sciences*, *110*(48), 19324–19329. https://doi.org/10.1073/pnas.1306373110

Kollarczik, B., Gareis, M., & Hanelt, M. (1994). In vitro transformation of the *Fusarium* mycotoxins deoxynivalenol and zearalenone by the normal gut microflora of pigs. *Natural Toxins*, *2*(3), 105–110. https://doi.org/10.1002/nt.2620020303

Kolosova, A., & Stroka, J. (2011). Substances for reduction of the contamination of feed by mycotoxins: A review. *World Mycotoxin Journal*, *4*(3), 225–256. https://doi.org/10.3920/WMJ2011.1288

Kong, C., Shin, S. Y., & Kim, B. G. (2014). Evaluation of mycotoxin sequestering agents for aflatoxin and deoxynivalenol: An in vitro approach. *SpringerPlus*, *3*(1), 346. https://doi.org/10.1186/2193-1801-3-346

Kostelanska, M., Dzuman, Z., Malachova, A., Capouchova, I., Prokinova, E., Skerikova, A., & Hajslova, J. (2011). Effects of milling and baking technologies on levels of deoxynivalenol and its masked form deoxynivalenol-3-glucoside. *Journal of Agricultural and Food Chemistry*, *59*(17), 9303–9312. https://doi.org/10.1021/jf202428f

Lancova, K., Hajslova, J., Kostelanska, M., Kohoutkova, J., Nedelnik, J., Moravcova, H., & Vanova, M. (2008). Fate of trichothecene mycotoxins during the processing: Milling and baking. *Food Additives & Contaminants*, *25*(5), 650–659. https://doi.org/10.1080/02652030701660536

Lancova, K., Hajslova, J., Poustka, J., Krplova, A., Zachariasova, M., Dostálek, P., & Sachambula, L. (2008). Transfer of *Fusarium* mycotoxins and 'masked'deoxynivalenol (deoxynivalenol-3-glucoside) from field barley through malt to beer. *Food Additives & Contaminants*, *25*(6), 732–744. https://doi.org/10.1080/02652030701779625

Li, X., Guo, Y., Zhao, L., Fan, Y., Ji, C., Zhang, J., & Ma, Q. (2018). Protective effects of Devosia sp. ANSB714 on growth performance, immunity function, antioxidant capacity and tissue residues in growing-finishing pigs fed with deoxynivalenol contaminated diets. *Food and Chemical Toxicology*, *121*, 246–251. https://doi.org/10.1016/j.fct.2018.09.007

Li, X., Shin, S., Heinen, S., Dill-Macky, R., Berthiller, F., Nersesian, N., … Muehlbauer, G. J. (2015). Transgenic wheat expressing a barley UDP-glucosyltransferase detoxifies deoxynivalenol and provides high levels of resistance to *Fusarium graminearum*. *Molecular Plant-Microbe Interactions*, *28*(11), 1237–1246. https://doi.org/10.1094/MPMI-03-15-0062-R

Li, X.-Z., Zhu, C., de Lange, C., Zhou, T., He, J., Yu, H., … Young, J. (2011). Efficacy of detoxification of deoxynivalenol-contaminated corn by Bacillus sp. LS100 in reducing the adverse effects of the mycotoxin on swine growth performance. *Food Additives & Contaminants: Part A*, *28*(7), 894–901. https://doi.org/10.1080/19440049.2011.576402

Liu, N., Yang, L., Yang, W., Jiang, S., Zhang, G., Niu, Q., … Yang, Z. (2016). Effects of feeding naturally contaminated diet with zearalenone, fumonisin and deoxynivalenol with or without yeast cell wall adsorbent on growth, vulva size and organ weights of gilts.

Journal of Animal and Feed Sciences, *25*(2), 145–151. https://doi.org/10.22358/jafs/65574/2016

Loi, M., Fanelli, F., Liuzzi, V. C., Logrieco, A. F., & Mulè, G. (2017). Mycotoxin biotransformation by native and commercial enzymes: Present and future perspectives. *Toxins*, *9*(4), 111. https://doi.org/10.3390/toxins9040111

Luz, W. C. D., Stockwell, C. A., Bergstrom, G. C., Leonard, K. J., & Bushnell, W. R. (2003). Biological control of *Fusarium graminearum*. In K. J. Leonard & W. R. Bushnell (Eds.), *Fusarium head blight of wheat and barley* (pp. 381–394). Saint Paul, MN: APS Press.

Machado, A. K., Brown, N. A., Urban, M., Kanyuka, K., & Hammond-Kosack, K. E. (2018). RNAi as an emerging approach to control *Fusarium* head blight disease and mycotoxin contamination in cereals. *Pest Management Science*, *74*(4), 790–799. https://doi.org/10.1002/ps.4748

Magallanes López, A. M., Manthey, F. A., & Simsek, S. (2019). Wet milling technique applied to deoxynivalenol-contaminated wheat dry-milled fractions. *Cereal Chemistry*, *96*(3), 487–496. https://doi.org/10.1002/cche.10148

Magnusson, J., & Schnürer, J. (2001). *Lactobacillus coryniformis* subsp. *coryniformis* strain Si3 produces a broad-spectrum proteinaceous antifungal compound. *Applied and Environmental Microbiology*, *67*(1), 1–5. https://doi.org/10.1128/AEM.67.1.1-5.2001

Magnusson, J., Ström, K., Roos, S., Sjögren, J., & Schnürer, J. (2003). Broad and complex antifungal activity among environmental isolates of lactic acid bacteria. *FEMS Microbiology Letters*, *219*(1), 129–135. https://doi.org/10.1016/s0378-1097(02)01207-7

Majumdar, R., Rajasekaran, K., & Cary, J. W. (2017). RNA interference (RNAi) as a potential tool for control of mycotoxin contamination in crop plants: Concepts and considerations. *Frontiers in Plant Science*, *8*, 200. https://doi.org/10.3389/fpls.2017.00200

Maresca, M. (2013). From the gut to the brain: Journey and pathophysiological effects of the food-associated trichothecene mycotoxin deoxynivalenol. *Toxins*, *5*(4), 784–820. https://doi.org/10.3390/toxins5040784

Mayer, E., Novak, B., Springler, A., Schwartz-Zimmermann, H. E., Nagl, V., Reisinger, N., … Schatzmayr, G. (2017). Effects of deoxynivalenol (DON) and its microbial biotransformation product deepoxy-deoxynivalenol (DOM-1) on a trout, pig, mouse, and human cell line. *Mycotoxin Research*, *33*(4), 297–308. https://doi.org/10.1007/s12550-017-0289-7

Mengelers, M., Zeilmaker, M., Vidal, A., De Boevre, M., De Saeger, S., & Hoogenveen, R. (2019). Biomonitoring of deoxynivalenol and deoxynivalenol-3-glucoside in human volunteers: Renal excretion profiles. *Toxins*, *11*(8), 466. https://doi.org/10.3390/toxins11080466

Nagl, V., Schwartz, H., Krska, R., Moll, W.-D., Knasmüller, S., Ritzmann, M., … Berthiller, F. (2012). Metabolism of the masked mycotoxin deoxynivalenol-3-glucoside in rats. *Toxicology Letters*, *213*(3), 367–373. https://doi.org/10.1016/j.toxlet.2012.07.024

Nagl, V., Woechtl, B., Schwartz-Zimmermann, H. E., Hennig-Pauka, I., Moll, W.-D., Adam, G., & Berthiller, F. (2014). Metabolism of the masked mycotoxin deoxynivalenol-3-glucoside in pigs. *Toxicology Letters*, *229*(1), 190–197. https://doi.org/10.1016/j.toxlet.2014.06.032

Nagy, C. M., Fejer, S. N., Berek, L., Molnar, J., & Viskolcz, B. (2005). Hydrogen bondings in deoxynivalenol (DON) conformations-a density functional study. *Journal of Molecular Structure: THEOCHEM*, *726*(1-3), 55–59. https://doi.org/10.1016/j.theochem.2005.02.079

Nasri, T., Bosch, R. R., Ten Voorde, S., & Fink-Gremmels, J. (2006). Differential induction of apoptosis by type A and B trichothecenes in Jurkat T-lymphocytes. *Toxicology in Vitro*, *20*(6), 832–840. https://doi.org/10.1016/j.tiv.2006.01.003

Nathanail, A. V., Gibson, B., Han, L., Peltonen, K., Ollilainen, V., Jestoi, M., & Laitila, A. (2016). The lager yeast Saccharomyces pastorianus removes and transforms *Fusarium* trichothecene mycotoxins during fermentation of brewer's wort. *Food Chemistry*, *203*, 448–455. https://doi.org/10.1016/j.foodchem.2016.02.070

Neira, M., Pacin, A., Martinez, E., Moltó, G., & Resnik, S. (1997). The effects of bakery processing on natural deoxynivalenol contamination. *International Journal of Food Microbiology*, *37*(1), 21–25. https://doi.org/10.1016/S0168-1605(97)00038-X

Niderkorn, V., Morgavi, D. P., Pujos, E., Tissandier, A., & Boudra, H. (2007). Screening of fermentative bacteria for their ability to bind and biotransform deoxynivalenol, zearalenone and fumonisins in an in vitro simulated corn silage model. *Food Additives & Contaminants*, *24*(4), 406–415. https://doi.org/10.1080/02652030601101110

Niku-Paavola, M. L., Laitila, A., Mattila-Sandholm, T., & Haikara, A. (1999). New types of antimicrobial compounds produced by *Lactobacillus plantarum*. *Journal of Applied Microbiology*, *86*(1), 29–35. https://doi.org/10.1046/j.1365-2672.1999.00632.x

Numanoglu, E., Gökmen, V., Uygun, U., & Koksel, H. (2012). Thermal degradation of deoxynivalenol during maize bread baking. *Food Additives & Contaminants: Part A*, *29*(3), 423–430. https://doi.org/10.1080/19440049.2011.644812

Nuraida, L. (2015). A review: Health promoting lactic acid bacteria in traditional Indonesian fermented foods. *Food Science and Human Wellness*, *4*(2), 47–55. https://doi.org/10.1016/j.fshw.2015.06.001

Oueslati, S., Berrada, H., Manes, J., & Juan, C. (2018). Presence of mycotoxins in Tunisian infant foods samples and subsequent risk assessment. *Food Control*, *84*, 362–369. https://doi.org/10.1016/j.foodcont.2017.08.021

Palazzini, J. M., Dunlap, C. A., Bowman, M. J., & Chulze, S. N. (2016). Bacillus velezensis RC 218 as a biocontrol agent to reduce *Fusarium* head blight and deoxynivalenol accumulation: Genome sequencing and secondary metabolite cluster profiles. *Microbiological Research*, *192*, 30–36. https://doi.org/10.1016/j.micres.2016.06.002

Palazzini, J. M., Ramirez, M. L., Torres, A. M., & Chulze, S. N. (2007). Potential biocontrol agents for *Fusarium* head blight and deoxynivalenol production in wheat. *Crop Protection*, *26*(11), 1702–1710. https://doi.org/10.1016/j.cropro.2007.03.004

Park, I., Parnsen, W., Duarte, M., Yiannikouris, A., & Kim, S. (2017). Effects of modified yeast cell wall extract on gut health and growth of newly weaned pigs under chronic dietary challenges of aflatoxin, deoxynivalenol, and fumonisin. *Journal of Animal Science*, *95*, 200. https://doi.org/10.2527/asasann.2017.406

Pascari, X., Marín, S., Ramos, A. J., Molino, F., & Sanchis, V. (2018). Deoxynivalenol in cereal-based baby food production process. A review. *Food Control*, *99*, 11–20. https://doi.org/10.1016/j.foodcont.2018.12.014

Pasquet, J.-C., Changenet, V., Macadré, C., Boex-Fontvieille, E., Soulhat, C., Bouchabké-Coussa, O., … Saindrenan, P. (2016). A Brachypodium UDP-glycosyltransferase confers root tolerance to deoxynivalenol and resistance to *Fusarium* infection. *Plant Physiology*, *172*(1), 559–574. https://doi.org/10.1104/pp.16.00371

Paster, N., Menasherov, M., Lacey, J., & Fanelli, C. (1992). Synergism between methods for inhibiting the spoilage of damp maize during storage. *Postharvest Biology and*

Technology, *2*(2), 163–170. https://doi.org/10.1016/0925-5214(92)90019-L

Patience, J., Myers, A., Ensley, S., Jacobs, B., & Madson, D. (2014). Evaluation of two mycotoxin mitigation strategies in grow-finish swine diets containing corn dried distillers grains with solubles naturally contaminated with deoxynivalenol. *Journal of Animal Science*, *92*(2), 620–626. https://doi.org/10.2527/jas.2013-6238

Payros, D., Alassane-Kpembi, I., Pierron, A., Loiseau, N., Pinton, P., & Oswald, I. P. (2016). Toxicology of deoxynivalenol and its acetylated and modified forms. *Archives of Toxicology*, *90*(12), 2931–2957. https://doi.org/10.1007/s00204-016-1826-4

Perczak, A., Goliński, P., Bryła, M., & Waśkiewicz, A. (2018). The efficiency of lactic acid bacteria against pathogenic fungi and mycotoxins. *Archives of Industrial Hygiene and Toxicology*, *69*(1), 32–45. https://doi.org/10.2478/aiht-2018-69-3051

Pereira, V., Fernandes, J., & Cunha, S. (2015). Comparative assessment of three cleanup procedures after QuEChERS extraction for determination of trichothecenes (type A and type B) in processed cereal-based baby foods by GC-MS. *Food Chemistry*, *182*, 143–149. https://doi.org/10.1016/j.foodchem.2015.01.047

Pierron, A. (2016). *Toxicity of three biological derivatives of deoxynivalenol: Deepoxy-deoxynivalenol, 3-epi-deoxynivalenol and deoxynivalenol-3-glucoside on pigs*. Toulouse, France: Université Paul Sabatier-Toulouse III.

Pierron, A., Bracarense, A. P. F. L., Cossalter, A. M., Laffitte, J., Schwartz-Zimmermann, H. E., Schatzmayr, G., … Oswald, I. P. (2018). Deepoxy-deoxynivalenol retains some immune-modulatory properties of the parent molecule deoxynivalenol in piglets. *Archives of Toxicology*, *92*, 3381–3389. https://doi.org/10.1007/s00204-018-2293-x

Pierron, A., Mimoun, S., Murate, L. S., Loiseau, N., Lippi, Y., Bracarense, A.-P. F., … Moll, W.-D. (2016). Intestinal toxicity of the masked mycotoxin deoxynivalenol-3-β-D-glucoside. *Archives of Toxicology*, *90*(8), 2037–2046. https://doi.org/10.1007/s00204-015-1592-8

Pierron, A., Mimoun, S., Murate, L. S., Loiseau, N., Lippi, Y., Bracarense, A.-P. F., … Moll, W.-D. (2016). Microbial biotransformation of DON: Molecular basis for reduced toxicity. *Scientific Reports*, *6*, 29105. https://doi.org/10.1038/srep29105

Pinton, P., Tsybulskyy, D., Lucioli, J., Laffitte, J., Callu, P., Lyazhri, F., … Oswald, I. P. (2012). Toxicity of deoxynivalenol and its acetylated derivatives on the intestine: Differential effects on morphology, barrier function, tight junction proteins, and mitogen-activated protein kinases. *Toxicological Sciences*, *130*(1), 180–190. https://doi.org/10.1093/toxsci/kfs239

Pitt, J., Taniwaki, M. H., & Cole, M. (2013). Mycotoxin production in major crops as influenced by growing, harvesting, storage and processing, with emphasis on the achievement of Food Safety Objectives. *Food Control*, *32*(1), 205–215. https://doi.org/10.1016/j.foodcont.2012.11.023

Poppenberger, B., Berthiller, F., Lucyshyn, D., Sieberer, T., Schuhmacher, R., Krska, R., … Adam, G. (2003). Detoxification of the *Fusarium* mycotoxin deoxynivalenol by a UDP-glucosyltransferase from Arabidopsis thaliana. *Journal of Biological Chemistry*, *278*(48), 47905–47914. https://doi.org/10.1074/jbc.M307552200

Raiola, A., Tenore, G. C., Manyes, L., Meca, G., & Ritieni, A. (2015). Risk analysis of main mycotoxins occurring in food for children: An overview. *Food and Chemical Toxicology*, *84*, 169–180. https://doi.org/10.1016/j.fct.2015.08.023

Repečkienė, J., Levinskaitė, L., Paškevičius, A., & Raudonienė, V. (2013). Toxin-producing fungi on feed grains and application of yeasts for their detoxification. *Polish Journal of Veterinary Sciences*, *16*(2), 391–393. https://doi.org/10.2478/pjvs-2013-0054

Rychen, G., Aquilina, G., Azimonti, G., Bampidis, V., Lourdes Bastos, M., Bories, G., … Gropp, J. (2017). Safety and efficacy of microorganism DSM 11798 as a technological additive for all avian species. *EFSA Journal*, *15*(1). https://doi.org/10.2903/j.efsa.2017.4676

Samar, M., Neira, M., Resnik, S., & Pacin, A. (2001). Effect of fermentation on naturally occurring deoxynivalenol (DON) in Argentinean bread processing technology. *Food Additives & Contaminants*, *18*(11), 1004–1010. https://doi.org/10.1080/02652030110051284

Samar, M., Resnik, S., Gonzalez, H., Pacin, A., & Castillo, M. (2007). Deoxynivalenol reduction during the frying process of turnover pie covers. *Food Control*, *18*(10), 1295–1299. https://doi.org/10.1016/j.foodcont.2006.08.008

Samarajeewa, U. (1991). In situ degradation of mycotoxins by physical methods. In J. E. Smith & R. S. Henderson (Eds.), *Mycotoxins and animal foods* (pp. 785–796). Boca Raton, FL: CRC Press.

Sato, I., Ito, M., Ishizaka, M., Ikunaga, Y., Sato, Y., Yoshida, S., … Tsushima, S. (2012). Thirteen novel deoxynivalenol-degrading bacteria are classified within two genera with distinct degradation mechanisms. *FEMS Microbiology Letters*, *327*(2), 110–117. https://doi.org/10.1111/j.1574-6968.2011.02461.x

Schnürer, J., & Magnusson, J. (2005). Antifungal lactic acid bacteria as biopreservatives. *Trends in Food Science & Technology*, *16*(1-3), 70–78. https://doi.org/10.1016/j.tifs.2004.02.014

Schwartz-Zimmermann, H., Fruhmann, P., Dänicke, S., Wiesenberger, G., Caha, S., Weber, J., & Berthiller, F. (2015). Metabolism of deoxynivalenol and deepoxy-deoxynivalenol in broiler chickens, pullets, roosters and turkeys. *Toxins*, *7*(11), 4706–4729. https://doi.org/10.3390/toxins7114706

Scudamore, K., Hazel, C. M., Patel, S., & Scriven, F. (2009). Deoxynivalenol and other *Fusarium* mycotoxins in bread, cake, and biscuits produced from UK-grown wheat under commercial and pilot scale conditions. *Food Additives & Contaminants*, *26*(8), 1191–1198. https://doi.org/10.1080/02652030902919426

Shetty, P. H., & Jespersen, L. (2006). Saccharomyces cerevisiae and lactic acid bacteria as potential mycotoxin decontaminating agents. *Trends in Food Science & Technology*, *17*(2), 48–55. https://doi.org/10.1016/j.tifs.2005.10.004

Shi, C., Yan, P., Li, J., Wu, H., Li, Q., & Guan, S. (2014). Biocontrol of *Fusarium graminearum* growth and deoxynivalenol production in wheat kernels with bacterial antagonists. *International Journal of Environmental Research and Public Health*, *11*(1), 1094–1105. https://doi.org/10.3390/ijerph110101094

Shima, J., Takase, S., Takahashi, Y., Iwai, Y., Fujimoto, H., Yamazaki, M., & Ochi, K. (1997). Novel detoxification of the trichothecene mycotoxin deoxynivalenol by a soil bacterium isolated by enrichment culture. *Applied and Environmental Microbiology*, *63*(10), 3825–3830. https://doi.org/10.1089/oli.1.1997.7.523

Simsek, S., Burgess, K., Whitney, K. L., Gu, Y., & Qian, S. Y. (2012). Analysis of deoxynivalenol and deoxynivalenol-3-glucoside in wheat. *Food Control*, *26*(2), 287–292. https://doi.org/10.1016/j.foodcont.2012.01.056

Springler, A., Hessenberger, S., Reisinger, N., Kern, C., Nagl, V., Schatzmayr, G., & Mayer, E. (2017). Deoxynivalenol and its metabolite deepoxy-deoxynivalenol: Multi-parameter analysis for the

evaluation of cytotoxicity and cellular effects. *Mycotoxin Research*, *33*(1), 25–37. https://xs.scihub.ltd/https://doi.org/10.1007/s12550-016-0260-z

Stadler, D., Lambertini, F., Bueschl, C., Wiesenberger, G., Hametner, C., Schwartz-Zimmermann, H., … Schuhmacher, R. (2019). Untargeted LC–MS based 13C labelling provides a full mass balance of deoxynivalenol and its degradation products formed during baking of crackers, biscuits and bread. *Food Chemistry*, *279*, 303–311. https://doi.org/10.1016/j.foodchem.2018.11.150

Streit, E., Naehrer, K., Rodrigues, I., & Schatzmayr, G. (2013). Mycotoxin occurrence in feed and feed raw materials worldwide: Long-term analysis with special focus on Europe and Asia. *Journal of the Science of Food and Agriculture*, *93*(12), 2892–2899. https://doi.org/10.1002/jsfa.6225

Suman, M., & Generotti, S. (2015). Transformation of mycotoxins upon food processing: Masking, binding and degradation phenomena. In C. Dall'Asta & F. Berthiller (Eds.), *Masked mycotoxins in food: Formation, occurrence and toxicological relevance* (pp. 73–89). Cambridge, UK: RSC Publishing. https://doi.org/10.1039/9781782622574-00073

Suman, M., Manzitti, A., & Catellani, D. (2012). A design of experiments approach to studying deoxynivalenol and deoxynivalenol-3-glucoside evolution throughout industrial production of wholegrain crackers exploiting LC-MS/MS techniques. *World Mycotoxin Journal*, *5*(3), 241–249. https://doi.org/10.3920/WMJ2012.1422

Sundstøl Eriksen, G., & Pettersson, H. (2003). Lack of de-epoxidation of type B trichothecenes in incubates with human faeces. *Food Additives & Contaminants*, *20*(6), 579–582. https://doi.org/10.1080/0265203031000102573

Suzuki, T., & Iwahashi, Y. (2015). Low toxicity of deoxynivalenol-3-glucoside in microbial cells. *Toxins*, *7*(1), 187–200. https://doi.org/10.3390/toxins7010187

Swanson, S. P., Nicoletti, J., Rood, H. D., Jr., Buck, W. B., Cote, L. M., & Yoshizawa, T. (1987). Metabolism of three trichothecene mycotoxins, T-2 toxin, diacetoxyscirpenol and deoxynivalenol, by bovne rumen microorganisms. *Journal of Chromatography B: Biomedical Sciences and Applications*, *414*, 335–342.

Talas, F., Kalih, R., Miedaner, T., & McDonald, B. A. (2016). Genome-wide association study identifies novel candidate genes for aggressiveness, deoxynivalenol production, and azole sensitivity in natural field populations of *Fusarium graminearum*. *Molecular Plant-Microbe Interactions*, *29*(5), 417–430. https://doi.org/10.1094/MPMI-09-15-0218-R

Tan, H., Zhang, Z., Hu, Y., Wu, L., Liao, F., He, J., … Ren, Z. (2015). Isolation and characterization of *Pseudomonas otitidis* TH-N1 capable of degrading Zearalenone. *Food Control*, *47*, 285–290. https://doi.org/10.1016/j.foodcont.2014.07.013

Terciolo, C., Maresca, M., Pinton, P., & Oswald, I. P. (2018). Role of satiety hormones in anorexia induction by trichothecene mycotoxins. *Food and Chemical Toxicology*, *121*, 701–714. https://doi.org/10.1016/j.fct.2018.09.034

Tian, Y., Tan, Y., Liu, N., Liao, Y., Sun, C., Wang, S., & Wu, A. (2016). Functional agents to biologically control deoxynivalenol contamination in cereal grains. *Frontiers in Microbiology*, *7*, 395. https://doi.org/10.3389/fmicb.2016.00395

Tibola, C. S., Fernandes, J. M. C., & Guarienti, E. M. (2016). Effect of cleaning, sorting and milling processes in wheat mycotoxin content. *Food Control*, *60*, 174–179. https://doi.org/10.1016/j.foodcont.2015.07.031

Tiwari, M., Sharma, D., & Trivedi, P. K. (2014). Artificial microRNA mediated gene silencing in plants: Progress and perspectives. *Plant Molecular Biology*, *86*(1-2), 1–18. https://doi.org/10.1007/s11103-014-0224-7

Ueno, Y. (1984). Toxicological features of T-2 toxin and related trichothecenes. *Toxicological Sciences*, *4*(2part2), 124–132.

Valgaeren, B., Théron, L., Croubels, S., Devreese, M., De Baere, S., Van Pamel, E., … Vidal, A. (2019). The role of roughage provision on the absorption and disposition of the mycotoxin deoxynivalenol and its acetylated derivatives in calves: From field observations to toxicokinetics. *Archives of Toxicology*, *93*(2), 293–310. https://xs.scihub.ltd/https://doi.org/10.1007/s00204-018-2368-8

Valle-Algarra, F. M., Mateo, E. M., Medina, A., Mateo, F., Gimeno-Adelantado, J. V., & Jiménez, M. (2009). Changes in ochratoxin A and type B trichothecenes contained in wheat flour during dough fermentation and bread-baking. *Food Additives & Contaminants*, *26*(6), 896–906. https://doi.org/10.1080/02652030902788938

van Egmond, H. P., Schothorst, R. C., & Jonker, M. A. (2007). Regulations relating to mycotoxins in food. *Analytical and Bioanalytical Chemistry*, *389*(1), 147–157. https://xs.scihub.ltd/https://doi.org/10.1007/s00216-007-1317-9

Vanhoutte, I., Audenaert, K., & De Gelder, L. (2018). *The quest for bacteria capable of detoxifying deoxynivalenol, a worldwide prevalent mycotoxin in cereal crops*. Retrieved from http://hdl.handle.net/1854/LU-8579033

Varga, E., Malachova, A., Schwartz, H., Krska, R., & Berthiller, F. (2013). Survey of deoxynivalenol and its conjugates deoxynivalenol-3-glucoside and 3-acetyl-deoxynivalenol in 374 beer samples. *Food Additives & Contaminants: Part A*, *30*(1), 137–146. https://doi.org/10.1080/19440049.2012.726745

Vidal, A., Ambrosio, A., Sanchis, V., Ramos, A. J., & Marín, S. (2016). Enzyme bread improvers affect the stability of deoxynivalenol and deoxynivalenol-3-glucoside during breadmaking. *Food Chemistry*, *208*, 288–296. https://doi.org/10.1016/j.foodchem.2016.04.003

Vidal, A., Marín, S., Morales, H., Ramos, A., & Sanchis, V. (2014). The fate of deoxynivalenol and ochratoxin A during the breadmaking process, effects of sourdough use and bran content. *Food and Chemical Toxicology*, *68*, 53–60. https://doi.org/10.1016/j.fct.2014.03.006

Vidal, A., Morales, H., Sanchis, V., Ramos, A. J., & Marín, S. (2014). Stability of DON and OTA during the breadmaking process and determination of process and performance criteria. *Food Control*, *40*, 234–242. https://doi.org/10.1016/j.foodcont.2013.11.044

Vidal, A., Sanchis, V., Ramos, A. J., & Marín, S. (2015). Thermal stability and kinetics of degradation of deoxynivalenol, deoxynivalenol conjugates and ochratoxin A during baking of wheat bakery products. *Food Chemistry*, *178*, 276–286. https://doi.org/10.1016/j.foodchem.2015.01.098

Vidal, A., Sanchis, V., Ramos, A. J., & Marin, S. (2016). The fate of deoxynivalenol through wheat processing to food products. *Current Opinion in Food Science*, *11*, 34–39. https://doi.org/10.1016/j.cofs.2016.09.001

Vidal, A., Sanchis, V., Ramos, A. J., & Marín, S. (2017). Effect of xylanase and α-amylase on DON and its conjugates during the breadmaking process. *Food Research International*, *101*, 139–147. https://doi.org/10.1016/j.foodres.2017.08.021

Vidal, A., Sanchis, V., Ramos, A. J., & Marín, S. (2018). Stability of DON and DON-3-glucoside during baking as affected by the presence of food additives. *Food Additives & Contaminants: Part A*, *35*(3), 529–537. https://doi.org/10.1080/19440049.2017.1401741

Visconti, A., Minervini, F., Lucivero, G., & Gambatesa, V. (1991). Cytotoxic and immunotoxic effects of *Fusarium* mycotoxins using a rapid colorimetric bioassay. *Mycopathologia*, *113*(3), 181–186.

Völkl, A., Vogler, B., Schollenberger, M., & Karlovsky, P. (2004). Microbial detoxification of mycotoxin deoxynivalenol. *Journal of Basic Microbiology: An International Journal on Biochemistry, Physiology, Genetics, Morphology, and Ecology of Microorganisms*, *44*(2), 147–156. https://doi.org/10.1002/jobm.200310353

Wang, G., Wang, Y., Ji, F., Xu, L., Yu, M., Shi, J., & Xu, J. (2019). Biodegradation of deoxynivalenol and its derivatives by Devosia insulae A16. *Food Chemistry*, *276*, 436–442. https://doi.org/10.1016/j.foodchem.2018.10.011

Westby, A., Reilly, A., & Bainbridge, Z. (1997). Fermentation on naturally occurring toxins. *Food Control*, *8*(5/6), 329–339. https://doi.org/10.1016/S0956-7135(97)00003-0

Westlake, K., Mackie, R. I., & Dutton, M. (1989). In vitro metabolism of mycotoxins by bacterial, protozoal and ovine ruminal fluid preparations. *Animal Feed Science and Technology*, *25*(1-2), 169–178. https://doi.org/10.1016/0377-8401(89)90117-X

Wolfhall, C. E., & Schwarz, P. B. (2002). Mycotoxins and fermentation—Beer production. In J. W. DeVries, M. W. Trucksess, & L. S. Jackson (Eds.), *Advances in experimental medicine & biology* (Vol. *504*, pp. 217–226). Boston, MA: Springer. https://doi.org/10.1007/978-1-4615-0629-4_22

Wood, B. J. (2012). *Microbiology of fermented foods*. Berlin, Germany: Springer Science & Business Media.

Wu, L., & Wang, B. (2015). Evaluation on levels and conversion profiles of DON, 3-ADON, and 15-ADON during bread making process. *Food Chemistry*, *185*, 509–516. https://doi.org/10.1016/j.foodchem.2015.03.082

Wu, W., He, K., Zhou, H.-R., Berthiller, F., Adam, G., Sugita-Konishi, Y., … Zhang, H. (2014). Effects of oral exposure to naturally-occurring and synthetic deoxynivalenol congeners on proinflammatory cytokine and chemokine mRNA expression in the mouse. *Toxicology and Applied Pharmacology*, *278*(2), 107–115. https://doi.org/10.1016/j.taap.2014.04.016

Wu, W., Zhou, H.-R., Bursian, S. J., Pan, X., Link, J. E., Berthiller, F., … Pestka, J. J. (2014). Comparison of anorectic and emetic potencies of deoxynivalenol (vomitoxin) to the plant metabolite deoxynivalenol-3-glucoside and synthetic deoxynivalenol derivatives EN139528 and EN139544. *Toxicological Sciences*, *142*(1), 167–181. https://doi.org/10.1093/toxsci/kfu166

Xu, J., Ji, F., Wang, H., Wang, J., Lin, F., & Shi, J. (2010). Isolation and identification of deoxynivalenol degradation strains. *Scientia Agricultura Sinica*, *43*(22), 4635–4641.

Xu, J., Pan, Y., Hu, X., Ji, F., Yin, X., & Shi, J. (2013). Enzymatic characteristics of 3-Acetyl deoxynivalenol oxidase by Devosia sp. DDS-1. *Scientia Agricultura Sinica*, *46*, 2240–2248.

Yang, X., Li, L., Duan, Y., & Yang, X. (2017). Antioxidant activity of Lactobacillus plantarum JM113 in vitro and its protective effect on broiler chickens challenged with deoxynivalenol. *Journal of Animal Science*, *95*(2), 837–846. https://doi.org/10.2527/jas.2016.0789

Yang, Y., Yu, S., Tan, Y., Liu, N., & Wu, A. (2017). Individual and combined cytotoxic effects of co-occurring deoxynivalenol family mycotoxins on human gastric epithelial cells. *Toxins*, *9*(3), 96. https://doi.org/10.3390/toxins9030096

Yoshizawa, T., Takeda, H., & Ohi, T. (1983). Structure of a novel metabolite from deoxynivalenol, a trichothecene mycotoxin, in animals. *Agricultural and Biological Chemistry*, *47*(9), 2133–2135. https://doi.org/10.1271/bbb1961.47.2133

Young, J. C., Zhou, T., Yu, H., Zhu, H., & Gong, J. (2007). Degradation of trichothecene mycotoxins by chicken intestinal microbes. *Food and Chemical Toxicology*, *45*(1), 136–143. https://doi.org/10.1016/j.fct.2006.07.028

Yu, H., Zhou, T., Gong, J., Young, C., Su, X., Li, X.-Z., … Yang, R. (2010). Isolation of deoxynivalenol-transforming bacteria from the chicken intestines using the approach of PCR-DGGE guided microbial selection. *BMC Microbiology*, *10*(1), 182. https://doi.org/10.1186/1471-2180-10-182

Yumbe-Guevara, B. E., Imoto, T., & Yoshizawa, T. (2003). Effects of heating procedures on deoxynivalenol, nivalenol and zearalenone levels in naturally contaminated barley and wheat. *Food Additives & Contaminants*, *20*(12), 1132–1140. https://doi.org/10.1080/02652030310001620432

Zannini, E., Waters, D. M., Coffey, A., & Arendt, E. K. (2016). Production, properties, and industrial food application of lactic acid bacteria-derived exopolysaccharides. *Applied Microbiology and Biotechnology*, *100*(3), 1121–1135. https://doi.org/10.1007/s00253-015-7172-2

Zeidan, R., Ul-Hassan, Z., Al-Thani, R., Balmas, V., & Jaoua, S. (2018). Application of low-fermenting yeast *Lachancea thermotolerans* for the control of toxigenic fungi *Aspergillus parasiticus*, *Penicillium verrucosum*, and *Fusarium graminearum* and their mycotoxins. *Toxins*, *10*(6), 242. https://doi.org/10.3390/toxins10060242

Zhang, X., Jiang, L., Geng, C., Cao, J., & Zhong, L. (2009). The role of oxidative stress in deoxynivalenol-induced DNA damage in HepG2 cells. *Toxicon*, *54*(4), 513–518. https://doi.org/10.1016/j.toxicon.2009.05.021

Zhang, Z., Nie, D., Fan, K., Yang, J., Guo, W., Meng, J., … Han, Z. (2019). A systematic review of plant-conjugated masked mycotoxins: Occurrence, toxicology, and metabolism. *Critical Reviews in Food Science and Nutrition*. https://doi.org/10.1080/10408398.2019.1578944

Zhao, L., Li, X., Ji, C., Rong, X., Liu, S., Zhang, J., & Ma, Q. (2016). Protective effect of Devosia sp. ANSB714 on growth performance, serum chemistry, immunity function and residues in kidneys of mice exposed to deoxynivalenol. *Food and Chemical Toxicology*, *92*, 143–149. https://doi.org/10.1016/j.fct.2016.03.020

Zhu, Y., Hassan, Y., Lepp, D., Shao, S., & Zhou, T. (2017). Strategies and methodologies for developing microbial detoxification systems to mitigate mycotoxins. *Toxins*, *9*(4), 130. https://doi.org/10.3390/toxins9040130

Zou, Z.-Y., He, Z.-F., Li, H.-J., Han, P.-F., Meng, X., Zhang, Y., … Tang, J. (2012). In vitro removal of deoxynivalenol and T-2 toxin by lactic acid bacteria. *Food Science and Biotechnology*, *21*(6), 1677–1683. https://doi.org/10.1007

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How to cite this article: Guo H, Ji J, Wang J-s, Sun X. Deoxynivalenol: Masked forms, fate during food processing, and potential biological remedies. *Compr Rev Food Sci Food Saf*. 2020;19:895–926. https://doi.org/10.1111/1541-4337.12545