frontiers in Microbiology

REVIEW
published: 25 April 2016
doi: 10.3389/fmicb.2016.00561

Biodegradation of Mycotoxins: Tales from Known and Unexplored Worlds

*Ilse Vanhoutte, Kris Audenaert and Leen De Gelder**

Department of Applied BioSciences, Faculty Bioscience Engineering, Ghent University, Ghent, Belgium

Exposure to mycotoxins, secondary metabolites produced by fungi, may infer serious risks for animal and human health and lead to economic losses. Several approaches to reduce these mycotoxins have been investigated such as chemical removal, physical binding, or microbial degradation. This review focuses on the microbial degradation or transformation of mycotoxins, with specific attention to the actual detoxification mechanisms of the mother compound. Furthermore, based on the similarities in chemical structure between groups of mycotoxins and environmentally recalcitrant compounds, known biodegradation pathways and degrading organisms which hold promise for the degradation of mycotoxins are presented.

Keywords: detoxification, microorganisms, mycotoxins, biodegradation, metabolite

OPEN ACCESS

Edited by:
Daniela Gwiazdowska, Poznan University of Economics, Poland

Reviewed by:
Augusto Schrank, Federal University of Rio Grande do Sul, Brazil
Ozgur Bayram, Maynooth University, National University of Ireland Maynooth, Ireland

****Correspondence:***
Leen De Gelder
leen.degelder@ugent.be

Specialty section:
This article was submitted to Fungi and Their Interactions, a section of the journal Frontiers in Microbiology

Received: *29 January 2016*
Accepted: *04 April 2016*
Published: *25 April 2016*

Citation:
Vanhoutte I, Audenaert K and De Gelder L (2016) Biodegradation of Mycotoxins: Tales from Known and Unexplored Worlds. Front. Microbiol. 7:561. doi: 10.3389/fmicb.2016.00561

INTRODUCTION

The presence of mycotoxins is inherent to many food and feed products worldwide (Bhat et al., 2010; Marroquín-Cardona et al., 2014). Hallmarks of their presence and their impact on animal and human health are encountered throughout history. Ergotism, also known as "St. Anthony's fire" occurred in several areas in Europe during the tenth century (Schiff, 2006) and was caused by the consumption of rye containing ergot alkaloids, produced by the fungus *Claviceps purpurea* (Bové, 1970; Beardall and Miller, 1994). In Siberia, a delayed harvest due to the second world war resulted in grains heavily contaminated with trichothecenes produced by *Fusarium* spp. People later consuming the grain were afflicted with number of nonspecific disorders and mortality mounted up to 10% (Manahan, 2002). In 1962, 100,000 turkeys died in London of Turkey X disease, linked to aflatoxins from *Aspergillus flavus* (Binder, 2007). These examples mentioned above illustrate the acute impact of high loads of singular mycotoxins on human and animal health. However, longtime exposure to low concentrations of mycotoxins also entail chronic toxicities which often result in non-specific symptoms, difficult to track-and-trace down to mycotoxins. These toxicities include estrogenic gastrointestinal, urogenital, vascular, kidney, and nervous disorders. Some mycotoxins are carcinogenic or immuno-compromising, and as such also promote the development of infectious diseases (Peraica et al., 1999; Hussein and Brasel, 2001; Creppy, 2002; Richard, 2007; Da Rocha et al., 2014).

For many years the research community focused on the occurrence of singular mycotoxins but nowadays scientific interest shifts to studies involving multiple mycotoxins. This new approach is highly relevant as large scale multi-toxin surveys show that a number of mycotoxins tend to co-occur with other sometimes structurally not-related mycotoxins (Gerding et al., 2014; Storm et al., 2014; Vanheule et al., 2014; and many more). In addition, mycotoxins are known to have additive and synergistic effects on human- and animal health (Alassane-Kpembi et al., 2013; Klaric et al., 2013; Clarke et al., 2014).

Research efforts progressively increase to develop mitigation strategies based on risk monitoring, risk characterization, prevention, intervention, and remediation strategies for multiple mycotoxins, which start from critical points along the production chain comprising field, storage, processing, and transportation. However, monitoring and good agricultural, storage, and transportation practices along with an effective Hazard Analysis and Critical Control Point approach do not completely prevent mycotoxin presence in the food or feed chain (Bhat et al., 2010). Decontamination technologies then offer a last resort to salvage contaminated batches along the production chain.

Decontamination strategies to reduce mycotoxins in food- and feed commodities are technologically diverse and based on physical, chemical, or biochemical principles. Some physical processes aim to remove highly contaminated fractions from bulk material (Bullerman and Bianchini, 2007; Cheli et al., 2013; Kaushik, 2015) through sorting (Scudamore et al., 2007), milling (Castells et al., 2007; Khatibi et al., 2014), dehulling (Fandohan et al., 2006; Rios et al., 2009; Matumba et al., 2015), cleaning (van der Westhuizen et al., 2011), heating, irradiation, or combinational approaches (Fandohan et al., 2005; Matumba et al., 2015). Another physical removal strategy is the use of inorganic or organic mycotoxin binders (Ramos et al., 1996; Kolosova and Stroka, 2011). Although these adsorbing binders have some promising features, some may have adverse nutritional effects due to binding of vitamins and minerals (Huwig et al., 2001; Yiannikouris et al., 2006) or reducing the efficacy pharmacokinetics of antibiotics (De Mil et al., 2015).

Chemical remediation strategies involve the conversion of mycotoxins via chemical reactions. Ammoniation (Norred et al., 1991), alkaline hydrolysis, peroxidation, ozonation, and the use of bisulphites are reported to be effective on one or more mycotoxins but a detailed insight into the toxicity of eventual end products or the impact on palatability and nutritive quality is questionable.

Microbial based methods comprise mycotoxin decomposition, transformation, or adsorption. The latter strategy has already been mentioned under physical measures and will not be considered in detail in this review. Focus in this review will be on transformation and biodegradation of the main mycotoxins by microorganisms. Although there are some excellent reviews on biodegradation (Zinedine et al., 2007; Wu et al., 2009; Awad et al., 2010; Jard et al., 2011; Devreese et al., 2013; McCormick, 2013; Hathout and Aly, 2014; Adebo et al., 2015), this review is timely because of two reasons:

Firstly, studies often wrongly identify biodegradation with detoxification, or do not test for toxicity of potential metabolites. Indeed, not all transformation or degradation products are detoxification products. This is nicely illustrated for aflatoxins and zearalenone (ZEN). Aflatoxin M1 (AFM1) is the hydroxylated metabolite of AFB1 and is categorized as *possible carcinogenic to humans* (Group 2B) by the International Agency for Research on Cancer (IARC; IARC, 2002). Aflatoxicol (or aflatoxin R_0), a reduction product of AFB1, has been detected as degradation product by *Corynebacterium rubrum, Aspergillus niger, Trichoderma viride, Mucor ambiguous,* and *Dactylium dendroides* (Mann and Rehm, 1976; Wong and Hsieh, 1976). However, Karabulut et al. (2014) concluded that AFB1 and aflatoxicol have similar potency to form an exo-epoxide analog which can bind to DNA. Assessing the ZEN biodegradation capacity of several microorganisms, Hahn et al. (2015) found that many strains were able to convert ZEN to α- and/or β-ZEL, showing similar estrogenic activity compared to ZEN. Aerobic and anaerobic degradation to other uncharacterized metabolites with unidentified toxicity was obtained as well. These results demonstrate the importance of *in vitro* experiments to critically screen agents claiming mycotoxin detoxification.

Secondly, the available set of mycotoxin degrading microorganisms is limited and their performance is often doubtful when considering multiple mycotoxin degradation. This issue was also nicely illustrated by Hahn et al. (2015). Using an *in vitro* screening approach, 20 commercially available agents claiming mycotoxin detoxification were tested for their efficacy to inactivate and/or degrade the two structurally not related mycotoxins DON or ZEN. The majority of the agents were not effective or converted the toxins to equally toxic metabolites. Only one of the products efficiently inactivated or degraded the two considered mycotoxins under the tested conditions.

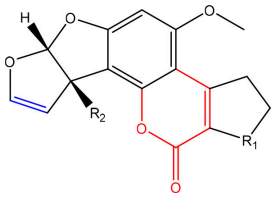
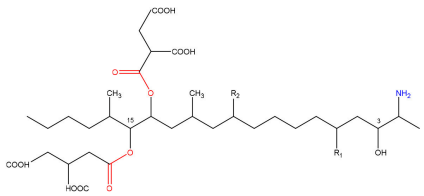
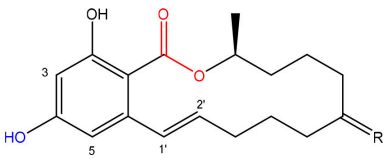
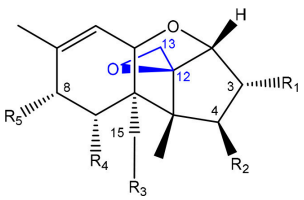
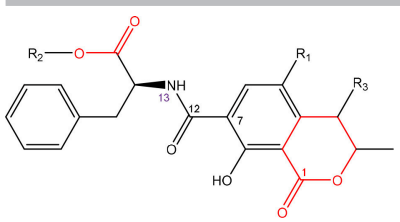
New insights on actual microbial detoxification routes are needed and can be based on known biodegradation metabolisms of non-mycotoxins found in diverse microbial communities, which we chose to identify as "unexplored worlds" to be discovered for the mycotoxin research field. Indeed, many hazardous, undesirable, deleterious, or recalcitrant molecules in other research fields share structural analogies with diverse mycotoxins and are reported to be successfully degraded by microorganisms. These unexplored worlds may serve as resource for cutting edge research in the field of mycotoxin remediation or in the field of metagenomics screening surveys in search for new microbial degraders of mycotoxins.

In this review, We are not only focusing on *Fusarium* mycotoxins, but also on *Aspergillus, Penicillium,* and other mycotoxins. This is relevant as independently of the producing genus, mycotoxins often share key-chemical groups responsible for their toxicity and thus biodegrading organisms for one mycotoxin can have their relevance for other mycotoxins produced by distinct fungal genera.

TOXICITY AND DEGRADATION OF MYCOTOXINS

In order to assess detoxification by microorganisms, it is important to pinpoint the actual groups within the chemical structure of each mycotoxin which infer the toxic effects (**Table 1**). Next to the main toxic structural groups occurring in mycotoxins, structural similarities between mycotoxins are also highlighted; aflatoxins and ochratoxins are both composed of a coumarin moiety, whereas the main structure of aflatoxins, ZEN and ochratoxins is based on a lactone ring (**Table 1**—Red). Carboxyl derivatives (ester bonds), often playing a role in toxicity, are frequently present, as well in the lactone, as in side groups (**Table 1**—Red) (observed in fumonisins, ZEN, ochratoxins, and acylated trichothecenes). Each mycotoxin is

TABLE 1 | Chemical structural groups inferring toxicity in mycotoxins.

Mycotoxin group	Side groups	Main toxic structural groups	References
AFLATOXINS			
	R_1 = C=O, -(C=O)-O- or C-OH	Lactone ring	Lee et al., 1981
	R_2 = H or OH	Double bond in difuran ring moiety	Wogan et al., 1971
FUMONISINS			
	R_1 = H or OH	Two tricarballylic acid side chains	Abbas et al., 1993b; Merrill et al., 1993b; Abbas et al., 1995; Voss et al., 1996b; Norred et al., 1997
	R_2 = H or OH	Free amino group	Abbas et al., 1993b; Norred et al., 1997
ZEARALENONES			
	R = O or H, α-OH	Lactone ring	El-sharkawy S. and Abul-hajj Y. J., 1988
	1',2' = trans or dihydro	C-4 hydroxyl group	El-sharkawy S. H. and Abul-hajj Y. J., 1988
TRICHOTHECENES			
	R_1 = H or OH	Epoxide group	Zhou et al., 2008
	R_2 = H, OH or OAc	Acylated side groups	Rocha et al., 2005
	R_3 = OH or OAc		
	R_4 = H or OH		
	R_5 = H, OH, =O, -O-(C=O)-CH2-CH-(CH3)2 or -O-(C=O)-CH2-COH-(CH3)2		
OCHRATOXINS			
	R_1 = Cl or H	Isocoumarin moiety	Xiao et al., 1996
	R_2 = H, methyl or ethyl	Carboxyl group of the phenylalanine moiety	
	R_3 = H or OH	Cl group	

Red, carboxylic derivatives (lactone rings and ester bonds) in red; Blue, specific groups responsible for toxicity.

further characterized concerning specific groups responsible for its toxicity (**Table 1**—Blue).

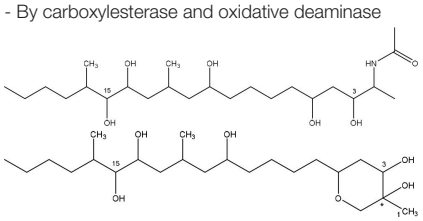
From our perspective, there are two ways in which detoxification of the mother compound in a degradation study can be confirmed: (i) the confirmation of reduced toxicity after degradation through one or more actual toxicity assays on particular organisms or cell lines, this is the most convincing proof; (ii) the detection and identification of detoxification products, for which in independent literature has been shown that they confer an lower toxicity to the mother compound. Of course, a combination of both ways provides the most holistic approach. The decreased toxicity of the degradation metabolites listed in **Tables 2**–**7** can therefore be found in **Table 1** in Supplementary Material.

Fumonisins

Toxicity

Fumonisins (most importantly FB1, FB2), first described by Gelderblom et al. (1988), are mainly produced by *F. verticillioides* and *F. proliferatum* and are structurally similar to sphingolipid long-chain bases such as sphinganine and sphingosine. This feature is tightly related to their toxicity mechanism through the inhibition of the sphingolipid biosynthesis (Merrill et al., 1993a; Soriano et al., 2005) and exposure to fumonisins

TABLE 2 | Degradation and/or detoxification products of fumonisins.

Degradation and/or detoxification product	Microorganism	References
REMOVAL OF TRICARBALLYLATE SIDE CHAINS AND AMINO GROUP		
- By carboxylesterase and aminotransferase	*Sphingomonas* sp. ATCC 55552*	Duvick et al., 1998a; Heinl et al., 2011 Patents: Duvick et al., 1998b, 2003
	Sphingopyxis sp. MTA 144	Täubel, 2005; Hartinger et al., 2009; Heinl et al., 2009, 2010 Patent: Moll et al., 2014
- By carboxylesterase and oxidative deaminase 	*Exophiala* sp*.	Duvick et al., 1998a; Blackwell et al., 1999 Patents: Duvick et al., 1998b, 2003
ACCUMULATION OF (TENTATIVELY) HEPTADECANONE, ISONONADECENE, OCTADECENAL AND EICOSANE		
	Delftia/Comomonas NCB 1492#	Benedetti et al., 2006
REMOVAL OF AMINO GROUP		
based on increased pH	*Bacillus* sp. and yeast strain	Camilo et al., 2000

*, *growth on fumonisin as sole carbon source.*
#, *growth on fumonisin as sole carbon and nitrogen source.*

has been associated a wide variety of diseases in animals as reviewed by Voss et al. (2007), such as liver cancer in rats, equine leukoencephalomalacia, and porcine pulmonary edema.

Specifically, fumonisins are comprised of a 22 carbon aminopentol with two tricarballylate (TCA) side groups, where two structural groups are important in their toxicity mechanism (**Table 1**). Firstly, the unsubstituted primary amino group at C2 competitively inhibits ceramide synthase, thereby disrupting the *de novo* biosynthesis of ceramide and sphingolipid metabolism (Voss et al., 2007). This free primary amino group of fumonisin-like compounds is a prerequisite for ceramide synthase inhibition, since N-acetylation of FB1 diminished or removed the toxicity effects in rat liver slices (Norred et al., 1997) and in jimsonweed and several mammalian cell lines (Abbas et al., 1993b). Secondly, the TCA side groups seem to have varying effects on the toxicity. On the one hand, absence of these side groups has been found to reduce both phytotoxicity and mammalian cytotoxicity (Abbas et al., 1995), and the resulting corresponding aminopentol (AP1, AP2) backbones were only 30–40% (Norred et al., 1997) or 10% as potent as the parent toxins (Merrill et al., 1993b). In contrast, removal of the TCA side groups has also been shown to enhance cytotoxicity in certain mammalian cell lines (Abbas et al., 1993b) and AP1 displays renal toxicity comparable to that of FB1 (Voss et al., 1996a).

Degradation: Organisms and Pathways

Only a few microorganisms are known to degrade and thereby detoxify fumonisins (**Table 2**), mostly by removal of the TCA groups as well as the free amino group. Although none of these studies actually determined detoxification of fumonisin B1 by these microorganisms through *in vitro* assays, based on what is known regarding the role of the TCA groups and the free amino group in inferring the toxicity of FB1 (**Table 1**, **Table 1** in Supplementary Material), we can safely assume detoxification was indeed achieved.

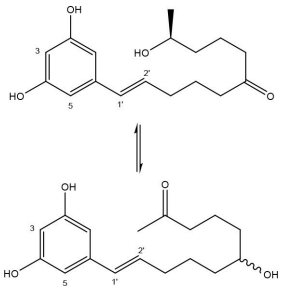
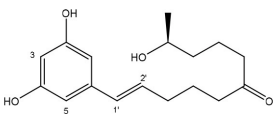
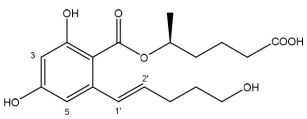
Sphingomonas sp. ATCC 55552 was isolated from field-grown, moldy maize kernels, and stalk tissue (Duvick et al., 1998a) and been shown to degrade fumonisin B1 through the consecutive action of a carboxylesterase (Duvick et al., 2003) and an aminotransferase (Heinl et al., 2011). The same pathway was found in *Sphingopyxis* sp. MTA 144 isolated from composted earth (Täubel, 2005), in which the gene cluster responsible for fumonisin degradation was identified with *fumD*, encoding the carboxylesterase and *fumI* encoding the aminotransferase (Hartinger et al., 2009; Heinl et al., 2009, 2010).

Degradation by *Exophiala* sp., also isolated from field-grown, moldy maize kernels, and stalk tissue (Duvick et al., 1998a), was shown to be conferred by a carboxylesterase and, in contrast to ATCC 55552 and MTA 144, by an oxidative deaminase. Two degradation products were identified: a new compound, 2-oxo-12,16-dimethyl-3,5,10,14,15-icosanepentol hemiketal, and in smaller amounts the N-acetylated aminopentol backbone (N-acetylAP1).

Strain NCB 1492, isolated from maize field soil and related to the *Delftia/Comamonas* group, gave rise to four tentative degradation products of fumonisin B1 ($C_{34}H_{59}NO_{15}$): heptadecanone ($C_{17}H_{34}O$), isononadecene ($C_{19}H_{38}$), octadecenal ($C_{18}H_{34}O$), and eicosane ($C_{20}H_{42}$) (Benedetti et al., 2006). The first degradative steps are thought to occur extracellularly, with deamination (and possibly esterase) activities followed by a slower degradation of the aliphatic chain.

Insights into the detoxification of fumonisins can also be useful for mycotoxins produced by other fungal genera. In

TABLE 3 | Degradation and/or detoxification products of ZEN.

Degradation and/or detoxification product	Microorganism	References
CLEAVAGE OF THE LACTONE RING		
	*Gliocladium roseum* RRL1859	El-sharkawy S. and Abul-hajj Y. J., 1988
 with decarboxylation	*Clonostachys rosea* IFO 7063 (a near-isogenic strain of NRRL 1859)	Kakeya et al., 2002; Takahashi-Ando et al., 2004
No α-zearalenol and α-zearalanol observed, CO_2-emmission indicative of decarboxylation	Culture extract of *B. natto* ClCC 24640 and *B. subtilis* 168	Tinyiro et al., 2011
 No decarboxylation No α - nor β-zearalenol detected	*Trichosporon mycotoxinivorans*	Molnar et al., 2004; Vekiru et al., 2010
CLEAVAGE OF THE AROMATIC RING		
ZEN-A ZEN-B: cleaved aromatic ring reduced liver and kidney damage (rats)	*Aspergillus niger* strain FS10	Sun et al., 2014
ZEN-1 and ZEN-2: cleaved aromatic ring reduced estrogenic effects	*Acinetobacter* sp. SM04*	Yu et al., 2011a
REDUCED TOXICITY CONFIRMED (NO DETOXIFICATION PRODUCTS IDENTIFIED)		
Reduced toxicity of ZEN and α- and β- zearalenone to *Artemia salina*	*Pseudomonas* sp. ZEA-1*	Altalhi, 2007
Decrease or complete removal (K408) of estrogenic effects	*Rhodococcus* sp. *Rhodococcus pyridinivorans* K408	Kriszt et al., 2012; Cserháti et al., 2013; Krifaton et al., 2013
8′(S)-hydroxyzearalenone and 2,4-dimethoxyzearalenone: no binding to rat estrogen receptor	*Streptomyces rimosus*	El-sharkawy S. H. and Abul-hajj Y. J., 1988

**uses ZEN as sole carbon source.*

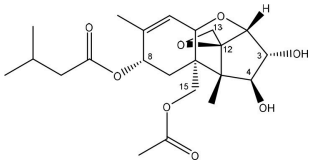
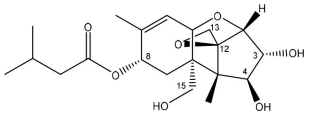
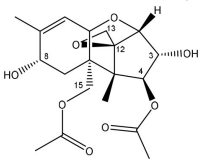
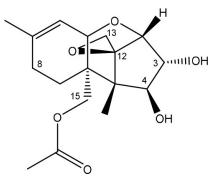
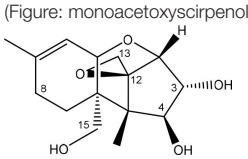
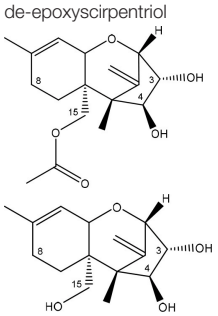
this light, we would like to draw the focus on the *Alternaria* toxins AAL-T_A en -T_B, which share with fumonisins a distinct structural similarity and toxicity mechanism (Abbas et al., 1993a; Tsuge et al., 2013). Fumonisins have two TCA side chains esterified to the aminopentol backbone, whereas AALtoxins have only one TCA side group, and are therefore collectively referred to as sphinganine-analog mycotoxins. To the best of our knowledge, there have not been any reports of microbial strains capable of degrading AAL-toxins, but based on their structural similarity it is likely that fumonisin degrading organisms as described above might also be capable of degrading AAL-toxin.

Zearalenone

Toxicity

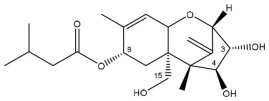
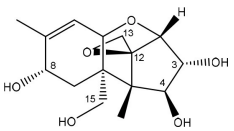
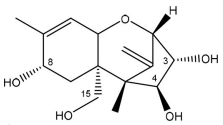
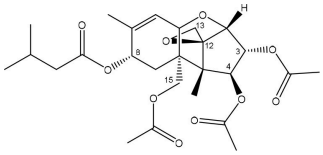
ZEN is mainly produced by fungi belonging to the genus *Fusarium* such as *F. graminearum* and *F. culmorum* and possesses estrogenic activity in pigs, cattle and sheep (Zinedine et al., 2007). The toxicity of ZEN is mainly conferred by its lactone group and the free C-4 hydroxyl group (**Table 1**) which is necessary for binding the estrogen receptor (El-sharkawy S. H. and Abul-hajj Y. J., 1988). Many derivatives of ZEN are known and some exhibit a higher estrogenicity than the mother compound (Shier et al., 2001), such as α-zearalenol, α- and β-zearalanol, and zearalanone. Several studies described the

TABLE 4 | Degradation and/or detoxification products of acylated trichothecenes.

Degradation and/or detoxification product	Microorganism	References
DEACETYLATION		
T-2 toxin → HT-2 toxin  (Figure: HT-2 toxin)	*Eubacterium* BBSH 797	Fuchs et al., 2002
	Carboxylesterase (from rat liver microsomes) (EC 3.1.1.1)	Ohta et al., 1977; Johnsen et al., 1986
T-2 toxin → HT-2 toxin → T-2 triol  (Figure: T-2 triol)	*Curtobacterium* sp. strain 114-2	Ueno et al., 1983
	Anaerovibrio lipolytica, *Selenomonas ruminantium*	Westlake et al., 1987
	Bacterial community from soil or freshwater	Beeton and Bull, 1989
T-2 toxin → HT-2 toxin, T-2 triol, neosolaniol  (Figure: neosolaniol)	*Butyrivibrio fibrisolvens* CE51	Westlake et al., 1987
T-2 toxin → neosolaniol	*Blastobotrys capitulata* strain	McCormick et al., 2012
Diacetoxyscirpenol → monoacetoxyscirpenol and scirpentriol  (Figure: monoacetoxyscirpenol)  (Figure: scirpentriol)	Fecal microflora from chickens, horses or dogs	Swanson et al., 1987
DAS → monoacetoxyscirpenol	*Butyrivibrio fibrisolvens* M-14a (from ovine rumen fluid)	Matsushima et al., 1996
DEACETYLATION AND DE-EPOXIDATION		
Diacetoxyscirpenol → de-epoxymonoacetoxyscirpenol and de-epoxyscirpentriol 	Mixed culture from intestinal microflora from rats	Swanson et al., 1987

(Continued)

TABLE 4 | Continued

Degradation and/or detoxification product	Microorganism	References
T-2 triol → 1. de-epoxy; 2. T-2 tetraol → 3. de-epoxy T-2 tetraol  1.  2.  3.	*Eubacterium* BBSH 797	Fuchs et al., 2002
DE-EPOXIDATION		
T-2 toxin → de-epoxy HT-2 toxin and de-epoxy T-2 triol	Mixed culture from intestinal microflora from rats	Swanson et al., 1987
HT-2 toxin → de-epoxy HT-2 toxin	*Eubacterium* BBSH 797	Fuchs et al., 2002
T-2 tetraol → de-epoxy T-2 tetraol	*Eubacterium* BBSH 797	Fuchs et al., 2002
3-ACETYLATION		
T-2 toxin → 3-acetyl T-2 toxin 	*Blastobotrys parvus* strain	McCormick et al., 2012

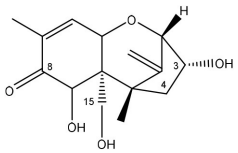
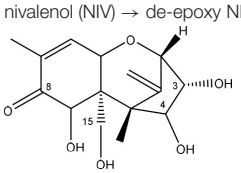
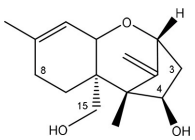
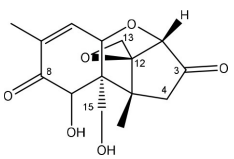
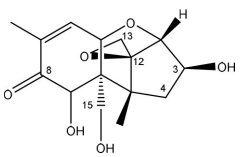
microbial transformation of ZEN to such derivatives, but as they do not represent a true detoxification of the compound they are not discussed in this review. Also, cases in which no clear evidence is presented (yet) for true detoxification (e.g., *Pseudomonas* strains in Tan et al., 2014, 2015) are not discussed in detail.

Degradation: Organisms and Pathways

To date, two main detoxification mechanisms are known for ZEN, both cleaving a ring structure (**Table 3**). The lactone ring can be cleaved by several fungal species through two mechanisms. Degradation by *Gliocladium roseum* NRRL1859 (El-sharkawy S. and Abul-hajj Y. J., 1988) resulted in a 1:1 mixture of 1-(3,5-dihydroxyphenyl)-10′-hydroxy-1-undecen-6′-one, and 1-(3,5-dihydroxyphenyl)-6′-hydroxy-1-undecen-10′-one. Matthies et al. (2001) showed that production of the ZEN-degrading enzyme in *G. roseum* DSM 62726 was induced the highest by the derivatives zearalanol and α-zearalanol. Almost similarly, only the first metabolite was observed after degradation by a near isogenic strain of NRRL1859, *Clonostachys rosea* (synonym: *G. roseum*, teleomorph: *Bionectria ochroleuca*) IFO 7063 (Kakeya et al., 2002), resulting in the loss of estrogenic activity in MCF-7 cancer cells (**Table 1** in Supplementary Materials), through the activity of a ZEN lactonohydrolase enzyme (zhd101) which catalyzes the hydrolysis of ZEN at the ester bond in the lactone ring, followed by spontaneous decarboxylation (Takahashi-Ando et al., 2004). Based on this knowledge, Popiel et al. (2014) searched a collection of *Trichoderma* and *Clonostachys* isolates for functional lactonohydrolase homologs, to find a functional ZEN lactonohydrolase in mycoparasitic *Trichoderma aggressivum*. A similar pathway might also exist in *Bacillus* sp., as cell culture extracts of *B. natto* CICC 24640 and *B. subtilis* 168 showed complete degradation of ZEN in conjunction with CO_2-emmission, indicative of decarboxylation (Tinyiro et al., 2011).

A second cleavage pathway is exhibited by the yeast *Trichosporum mycotoxinivorans* (Molnar et al., 2004) to ZOM-1 intermediate (cleavage at the C6-ketone group), suggested to take place through a lactone intermediate and subsequent activity by unspecified a/b-hydrolase, but without the decarboxylation as seen in *C. rosea.* ZOM-1 did not show any estrogenic activity in a yeast bioassay, nor interaction with the human estrogen receptor (Vekiru et al., 2010), nor estrogenic activity with MCF-7 cells (Liu et al., 2001). It is important to notice that *T. mycotoxinivorans* is well-known in medicine, since it can cause opportunistic infections or induce summer-type

TABLE 5 | Degradation and/or detoxification products of non-acylated tricothecenes.

Degradation and/or detoxification product	Microorganism	References
DE-EPOXIDATION		
DON → de-epoxy DON (DOM-1) 	*Eubacterium* BBSH 797 (anaerobically)	Binder and Binder, 2004
	Chicken intestinal microbes	Young et al., 2007
	Isolate from chicken guts	Zhou et al., 2007
	Microbial community C133 (from fish guts)	Guan et al., 2009
	Isolate LS-100 (99% ∼ *Bacillus arbutinivorans*) (from chicken intestines)	Yu et al., 2010
	Citrobacter freundii (aerobically)	Rafiqul, 2012
nivalenol (NIV) → de-epoxy NIV 	*Eubacterium* BBSH 797	Fuchs et al., 2000
	Chicken intestinal microbes	Young et al., 2007
	Microbial community C133 (from fish guts)	Guan et al., 2009
verrucarol → de-epoxy verrucarol 	Chicken intestinal microbes	Young et al., 2007
	Microbial community C133 (from fish guts)	Guan et al., 2009
C3 MODIFICATION THROUGH OXIDATION		
3-keto-DON 	*Agrobacterium-Rhizobium* strain E3-39 (soil)	Shima et al., 1997
	Mixed culture	Volkl et al., 2004
	Devosia mutans strain 17-2-E-8	He, 2015
C3 MODIFICATION THROUGH EPIMERIZATION		
3-epi-DON 	*Nocardioides* strain WSN05-2 (soil, wheat field)*	Ikunaga et al., 2011
	Nocardioides strains (environmental samples (field soils, wheat leaves))*	Sato et al., 2012
	Devosia strains (environmental samples (field soils, wheat leaves))	Sato et al., 2012
	Devosia mutans strain 17-2-E-8	He, 2015

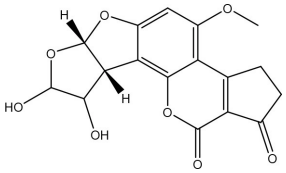
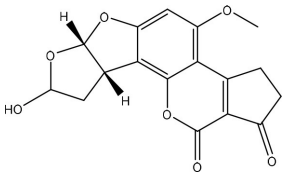
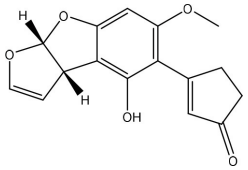
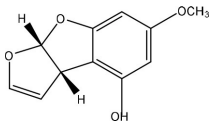
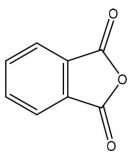
**growth as sole carbon source.*

hypersensitivity pneumonitis in immune-deficient cystic fibrosis patients (Tintelnot et al., 2011) which can be an impediment for applications.

Detoxification of ZEN contaminated corn steep liquor by *A. niger* strain FS10 and its culture filtrate, exemplified by less severe liver and kidney damage in rats, was recently reported (Sun et al., 2014). Two intermediate products, ZEN-A and ZEN-B, which inferred reduced liver and kidney damage in rats compared to ZEN, were detected, of which the latter the authors suggested the benzene ring might be cleaved because the UV absorption of ZEN was lost in ZEN-B. Somewhat similarly, two degradation products (ZEN-1 and ZEN-2) were detected after degradation by *Acinetobacter* sp. SM04 isolated from agricultural soil, for which no equally estrogenic activity could be detected on the basis of the MTT (tetrazolium salt) cell proliferation assay in MCF-7 cell line. Also, UV-Vis spectroscopy indicated cleavage of the benzene ring in these products (Yu et al., 2011a). Interestingly, ZEN and its estrogenic properties were only reduced when degradation tests were performed with extracellular extracts from M1 medium cultures, where sodium acetate is the only extra carbon source, and not from Nutrient Broth cultures, where many different extra carbon sources are present (Yu et al., 2011b). This indicates that the transcription of genes responsible for ZEN degradation may be regulated by catabolite repression.

Pseudomonas sp. ZEA-1, isolated from the rhizosphere of a corn plant, was shown to harbor the responsible degradation genes on a 120 kb plasmid mediating the transformation of ZEN and its derivatives α- and β- ZEN into less toxic products to *Artemia salina*. The transformation product was not elucidated,

TABLE 6 | Degradation and/or detoxification products of aflatoxins.

Degradation and/or detoxification product	Microorganism	References
AFB1-8,9-DIHYDRODIOL		
	*Armillariella tabescens* *Phanerochaete sordida*	Liu et al., 1998a,b Wang et al., 2011
AFB2a		
	*Pleurotus ostreatus* GHBBF10	Das et al., 2014 Wong and Hsieh, 1976
AFD1		
	*Pseudomonas putida*	Samuel et al., 2014 Grove et al., 1984
AFD2		
	*Pseudomonas putida*	Samuel et al., 2014
AFD3		
	*Pseudomonas putida*	Samuel et al., 2014
REDUCED TOXICITY CONFIRMED (NO DETOXIFICATION PRODUCTS IDENTIFIED)		
reduced mutagenicity	*Flavobacterium aurantiacum (= Nocardia corynebacterioides)*	Ciegler et al., 1966; Teniola et al., 2005
	laccase enzyme (*T. versicolor)* recombinant laccase enzyme *(A. niger)*	Alberts et al., 2009
	Rhodococcus erythropolis	Alberts et al., 2006
reduced genotoxicity with SOS-chromotest	several *Rhodococcus* sp.	Cserháti et al., 2013
reduced toxicity in *Aliivibrio fischeri* or with SOS-chromotest	several *Rhodococcus* sp. and *Pseudomonas* sp.	Krifaton et al., 2011

other than the specific absorption maximum at 400 nm (Altalhi, 2007). A 5.5 kb fragment containing the gene(s) encoding for ZEN degradation was cloned and actively expressed in *Escherichia coli* (Altalhi and El-Deeb, 2009).

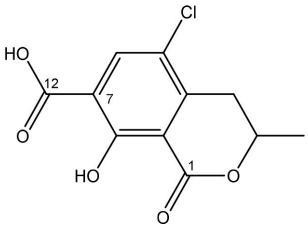
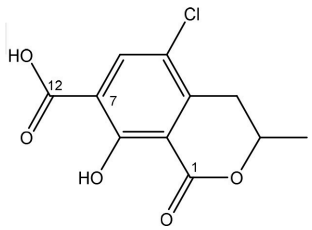
The complete loss of ZEN estrogenic activity was obtained by several degrading *Rhodococcus* strains (Kriszt et al., 2012; Cserháti et al., 2013), without the identification of possible metabolites. *R. pyridinovorans* K408 showed a biodegradation potential of up to 85% and decreased the estrogenicity with 76%. Several strains also simultaneously degraded AFB1, ZEN, and T2-toxin (Cserháti et al., 2013), confirming the status *Rhodococcus* as a metabolically highly versatile genus with a large potential for degradation of aromatic and other pollutants (Larkin et al., 2005).

Trichothecenes

Toxicity

Trichothecenes are sesquiterpenoids produced by mainly the genera *Fusarium*, *Trichothecium*, *Myrothecium, Trichoderma,* and *Stachybotrys* fungi (Sudakin, 2003; Kimura et al., 2007; Li

TABLE 7 | Degradation and/or detoxification products of ochratoxins.

Degradation/detoxification product	Microorganism	References
ENZYMATIC REMOVAL OF PHENYLALANINE GROUP	**BACTERIA**	
ochratoxin α 	*Bacillus licheniformis*	Petchkongkaew et al., 2008
	Bacillus spp.	
	Brevibacterium linens	Rodriguez et al., 2011
	Brevibacterium iodinum	
	Brevibacterium epidermidis	
	Acinetobacter calcoaceticus	Hwang and Draughon, 1994; De Bellis et al., 2015
	Penylobacterium immobile	Wegst and Lingens, 1983
	Bacillus amyloliquefaciens ASAG1	Chang et al., 2015
	Cupriavidus basilensis Or16	Ferenczi et al., 2014
	Pediococcus parvulus	Abrunhosa et al., 2014
	Lactobacillus acidophilus	Fuchs et al., 2008
ENZYMATIC REMOVAL OF PHENYLALANINE GROUP	**FUNGI**	
ochratoxin α 	*Aspergillus clavatus*	Abrunhosa et al., 2002; Bejaoui et al., 2006
	Aspergillus vesicolor	
	Aspergillus niger	
	Aspergillus japonicas	
	Aspergillus alliaceus	
	Aspergillus alliaceus	
	Aspergillus ochraceus	
	Aspergillus wentii	
	Trichosporon mycotoxinivorans	Molnar et al., 2004
	Botrytis spp	Abrunhosa et al., 2002
	Alternaria spp.	
	Penicillium spp.	
	Cladosporium spp.	
	Rhizopus spp	Varga et al., 2005
	Pleurotus ostreatus	Engelhardt, 2002
	Saccharomyces spp.	
	Rhodoturula spp.	
	Cryptococcus spp.	
	Pfaffia rhodozyma	Péteri et al., 2007
	Aureobasidium pullulans	de Felice et al., 2008
	Aspergillus niger	Dobritzsch et al., 2014
	Aspergillus niger	Stander et al., 2000

et al., 2011). High doses lead to emesis, whereas low doses induce decreased feed consumption and weight gain (Eriksen and Pettersson, 2004). Trichothecenes are characterized by a 12,13-epoxy-trichothec-9-ene nucleus (Hussein and Brasel, 2001). Type A trichothecenes do not contain carbonyl function at C8 (T-2 toxin, HT-2 toxin, T-2 tetraol, T-2 triol, 15-monoacetoxyscirpenol, DAS, neosolaniol, and scirpentriol). Type B trichothecenes have a carbonyl group at C8 [deoxynivalenol (DON), 15-acetyl DON, 3-acetyl DON, nivalenol (NIV), 4-acetyl NIV]. Type C trichothecenes include another epoxide group and type D trichothecenes contains an additional ring system between C4 and C15 position (Zhou et al., 2008; McCormick et al., 2011).

The 12,13-epoxide ring in trichothecenes is essential for their toxicity (Zhou et al., 2008) and has been linked to the cytotoxicity of trichothecenes, namely inhibition of protein, RNA and DNA synthesis (Hussein and Brasel, 2001; Rocha et al., 2005). Trichothecenes bind with the 60S subunit of the ribosome and interfere with the action of peptidyltransferase (Ehrlich and Daigle, 1987). However, the degree of toxicity is dependent on the presence of substituents on C15 and C4 (Cundliffe et al., 1974; Cundliffe and Davies, 1977). The most potent mycotoxin T-2 toxin has acetyl or acyl side groups on C4, C8, and C15 of the basic structure. Loss of a side group from either of these positions resulted in reduced protein synthesis inhibition (T-2 toxin to HT-2 toxin, neosolaniol, or DAS). Further removal of side groups weakens their effect (T-2 triol, T-2 tetraol, 15-monoacetyl DAS, scirpentriol, fusarenon X, and DON) and reduction of hydroxyl groups, forming verrucarol, reduced their effectiveness greatly (Thompson and Wannemacher, 1986; **Table 2** in Supplementary Material). De-acylation is clearly

a first step toward detoxification, illustrated in **Figure 1** in Supplementary Material. This reduced effect of de-acylation of T-2 toxin is also confirmed with human melanoma SK-Mel/27 cell lines (Babich and Borenfreund, 1991) and β-galactosidase activity of *Kluyveromyces marxianus* (Engler et al., 1999) showing the same tendency (**Table 1** in Supplementary Material).

Degradation: Organisms and Pathways

The toxicity of trichothecenes is, next to their epoxide-group, also dependent on their acylated side chains. Therefore, two main groups are distinguished; acylated (e.g., T-2 toxin) and non-acylated trichothecenes (e.g., DON).

As previously described, de-acylation is the first step in detoxification of acylated trichothecenes. Degradation of T-2 toxin to HT-2 toxin and subsequently to T-2 triol was performed by *Curtobacterium* sp. strain 114-2 of which the reduced toxicity of T-2 triol was once more confirmed resulting in 23 and 13 times less toxic than, respectively T-2 toxin and HT-2 toxin (Ueno et al., 1983; **Table 4**). Still, the epoxide group in trichothecenes remains responsible for their toxicity. De-epoxidation is the next step of detoxification trichothecenes. Several studies focuses on the degradation of multiple trichothecenes and the differences between their metabolism by the same organism(s). Young et al. (2007) studied the metabolism of diverse trichothecenes by chicken intestinal microbes. For the non-acylated trichothecenes (4-DON, NIV, and verrucarol) their de-epoxidized metabolites were observed, for DAS, neosolaniol and T-2 toxin only de-acylation was exhibited and for the monoacetyl trichothecenes (3-acetyl DON, 15-acetyl DON, and fusarenon X), de-acylation was the predominant pathway. In another study, pig gastrointestinal microflora transformed 3-acetyl DON into DON and which was further de-epoxidized (Eriksen et al., 2002). Rat intestinal microflora was also able to de-epoxidize T-2 tetraol and scirpentriol, transform T-2 toxin into de-epoxy HT-2 toxin and de-epoxy T-2 triol and DAS into de-epoxymonoacetoxyscirpenol and de-epoxyscirpentriol (Swanson et al., 1987). All above mentioned cases concern degradation by mixed cultures. In contrast, *Eubacterium* BBSH 797 has the ability to degrade several trichothecenes as pure culture isolated from bovine rumen fluid (Fuchs et al., 2000, 2002; Binder and Binder, 2004) and has been developed into a commercial product (Biomin® BBSH 797) for detoxifying trichothecenes in animal feed (He et al., 2010). It is known for its detoxification capacities of DON into DOM-1 and de-epoxidization of NIV, T-2 tetraol, scirpentriol, and HT-2 toxin. T-2 toxin was de-acylated into HT-2 toxin, whereas degradation of T-2 triol involved the competition of two reactions; (1) de-epoxidation or (2) deacylation into T-2 tetraol and subsequently de-epoxidation into de-epoxy T-2 tetraol (Fuchs et al., 2002). Further, 4-acetyl NIV and 3-acetyl NIV was de-acetylated and/or de-epoxidized (Fuchs et al., 2000).

Degradation of DON occurs through de-epoxidation, oxidation, or isomerization (**Table 5**). Microbial culture C133 of fish guts transformed DON to DOM-1 (Guan et al., 2009). *Eubacterium* BBSH 797 is known to degrade DON into DOM-1 anaerobically (Binder and Binder, 2004). *Citrobacter freundii* could transform DON into DOM-1 aerobically (Rafiqul, 2012). DON can also be oxidized to 3-keto DON which is 10 times less toxic than DON evaluated with a bioassay based on mitogen-induced and mitogen-free proliferations of mouse spleen lymphocytes (Shima et al., 1997). The bacterium strain E3-39 which degraded DON to 3-keto-DON, is belonging to the *Agrobacterium-Rhizobium* group. A mixed culture from environmental sources could degrade DON into 3-keto-DON, whereas 15-acetyl DON, 3-acetyl DON and fusarenon-X were also transformed (Volkl et al., 2004). Subsequently, He (2015) found the soil bacterium *Devosia mutans* 17-2-E-8 which transformed DON into 3-epi-DON (major product) and 3-keto-DON (minor product). These metabolites have also been tested on their toxicity with two assays. The IC_{50} values of 3-epi-DON and 3-keto-DON were 357 and 3 times higher, respectively, than that of DON on the basis of a MTT bioassay using Caco-2 cell line to asses cell viability, and were 1181 and 5 times higher, respectively, than that of DON on the basis of a cell proliferation BrdU bioassay using 3T3 fibroblast cell line to asses DNA synthesis (**Table 1** in Supplementary Material). Toxicological effects of 14-day oral exposure of $B6C3F_1$ mouse to DON and 3-epi-DON were also investigated concluding that 3-epi-DON was at least 50 times less toxic than DON (He, 2015). The metabolite 3-epi-DON was also formed by degradation of DON through *Nocardioides* sp. strain WSN05-2 isolated from a wheat field (Ikunaga et al., 2011). And lastly, nine *Nocardioides* strains (Gram-positive) and four *Devosia* strains (Gram-negative) produced 3-epi-DON aerobically. The Gram-positive strains showed DON assimilation, whereas the Gram-negatives did not (Sato et al., 2012).

Further, hydroxylation and glycosylation of trichothecenes are also known for their detoxification capability (He et al., 2010), however these derivatives can be rehydrolyzed or regenerated in the digestive tract of animals and humans losing their detoxification capacity.

Aflatoxins

Toxicity

Aflatoxins are furanocoumarins produced by mainly *Aspergillus* species (Wu et al., 2009; Samuel et al., 2013). Naturally occurring aflatoxins are categorized by IARC as carcinogenic to humans (Group 1; IARC, 2002). Aflatoxin B1 (AFB1) is activated by cytochrome P450 system to a highly reactive AFB1-8,9-epoxide which can react with DNA (Eaton and Groopman, 1994; Guengerich et al., 1996).

The toxicity of AFB1 is mainly caused by the lactone ring. Cleavage of the lactone ring leads to a non-fluorescent compound with reduced biological activity (Lee et al., 1981). The residual component has a 450 times reduced mutagenicity (measured with the Ames test) and a 18 times reduced toxicity (measured with chicken embryo test; Lee et al., 1981). Also the difuran ring moiety, especially the presence of the double bond in the terminal furan ring, contributes to the toxicity (Wogan et al., 1971) as evidenced by comparing the toxicity of aflatoxins with similar coumarin molecules. Wong and Hsieh (1976) concluded by comparing several aflatoxins and metabolites with the Ames test that the double bond was also involved in both mutagenic

and carcinogenic activity of aflatoxins leading that the aflatoxins AFB2 and AFG2 (without a double bond) are much less toxic than AFB1 and AFG1 (with a double bond).

Degradation: Organisms and Pathways

To our knowledge, a first report on the microbial detoxification of AFB1 has been published in 1966, mediated by *Flavobacterium aurantiacum* (now called *Nocardia corynebacterioides*; Ciegler et al., 1966; Teniola et al., 2005). Although no detoxification products were analyzed, residual toxicity to ducklings was found to be absent indicating true detoxification (Ciegler et al., 1966). The biosafety of the microorganism was confirmed using an *in vivo* trial with chickens (Tejada-Castañeda et al., 2008). Since this first report, many studies have focused on the detoxification of AFB1. However, only a few studies detected the degradation products and analyzed their toxicity. Generally, two main detoxification pathways are observed: modification of the difuran ring or modification of the coumarin structure.

Firstly, modification of the difuran ring moiety was reported in several studies. Degradation of AFB1 into AFB1-8,9-dihydrodiol was performed by manganese peroxidase from the white rot fungi *Phanerochaete sordida* (Wang et al., 2011) and the "aflatoxin-detoxifizyme (ADTZ)" of fungus *Armillariella tabescens* (Liu et al., 1998b; **Table 6**). The authors suggested that AFB1 degradation initially involves formation of AFB1-8,9-epoxide, after which a hydrolysis resulted in a dihydrodiol-derivate. Detoxification was confirmed with a reduced mutagenicity measured by the Ames *Salmonella*-based test (Liu et al., 1998b, 2001; Wang et al., 2011; **Table 1** in Supplementary Material) and reduced toxicity measured with rat liver (Liu et al., 1998b) and chicken embryos (Liu et al., 1998a). Another metabolite was detected with the white rot fungus *Pleurotus ostreatus* GHBBF10 which degraded 91.76% of AFB1 into a component which could be a hydrolyte of AFB1, namely dihydrohydroxyaflatoxin B1 (AFB2a) (Das et al., 2014; **Table 2**). AFB2a has also a reduced mutagenicity (Wong and Hsieh, 1976; **Table 1** in Supplementary Material).

Secondly, the lactone ring in the coumarin moiety of AFB1 can be changed. A *Pseudomonas putida* strain has been discovered degrading AFB1 into AFD1 and subsequently into AFD2 (**Table 6**). The metabolite AFD1 had been previously discovered through ammonization and acidifying AFB1, whereas the difuran ring stays unchanged and the lactone ring is cleaved. AFD1 has a lower mutagenicity and toxicity measured by respectively the Ames *Salmonella*-based test (Méndez-Albores et al., 2005) and HeLa cells with the MTT [3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide] method (Samuel et al., 2014). The metabolites AFD2 (an aflatoxin metabolite lacking the lactone and cyclopentenone ring) and AFD3 also showed a lower toxicity toward HeLa cells (**Table 1** in Supplementary Material; Samuel et al., 2014).

In certain studies, no degradation product was identified, but toxicity tests were performed on the treated AFB1. Similarly to *F. aurantiacum* as mentioned before, a pure laccase enzyme from *Trametes versicolor* and a recombinant laccase enzyme produced by *A. niger* degraded, respectively, 87.34 and 55% of AFB1 with a significant loss of mutagenicity evaluated in the Ames *Salmonella*-based assay (Alberts et al., 2009). Extracellular enzymes of *Rhodococcus eryhtropolis* were also able to detoxify AFB1 with a loss of mutagenicity (Alberts et al., 2006).

Ochratoxins

Toxicity

Ochratoxins (OT) are a group of mycotoxins sharing an isocoumarin moiety substituted with a phenylalanine group (OTA, OTB, hydroxyl-OTA), a phenylalanine ester group (OTC, OTA methylester, OTB methyl ester, OTB ethyl ester), or a hydroxyl group (OTα and OTβ). OTA is the most important OT because of its incidence in food- and feed commodities. It is composed of a 7-carboxy-5-chloro-8-hydroxy-3,4-dihydro-3-R-methylisocoumarin (OTα) moiety and the amino acid L- phenylalanine group. Both structures are linked through a carboxy group via an amide bond. OTA is produced by *Aspergillus* and *Penicillium* species (Richard, 2007; McCormick, 2013). The mode of action of OTA is broad and therefore the molecule has nephrotoxic, mutagenic, teratogenic, neurotoxic, hepatotoxic, and immunotoxic properties (Pfohl-Leszkowicz and Manderville, 2007). The toxicity of OTA is mainly attributed to its isocoumarin moiety and probably not to the phenylalanine moiety (**Table 1**; Xiao et al., 1996). The carboxyl group of the phenylalanine moiety and also the Cl group of the other moiety seem to be conducive for the toxicity of OTA.

Degradation: Organisms and Pathways

The main detoxification pathway of OTA is the hydrolyzation of the amide bond between the isocoumarin residue and phenylalanine by a carboxypeptidase. Two classes of carboxypeptidases have been associated with degradation of OTA namely Carboxypeptidase A (CPA) (Stander et al., 2001; Chang et al., 2015) and Y (CPY) (Dridi et al., 2015). The main difference between both is the use of a zinc ion within the protein for hydrolysis of the peptide at the C-terminal of the amino acid. Almost all strains that are reported to degrade OTA use this pathway resulting in the formation of L-β-phenylalanine and OTα the former being less toxic than OTA (**Table 7**; Bruinink and Sidler, 1997). Although this is a very straightforward way of reducing the amount of OTA in food and feed samples, it is important to highlight that the efficient degradation of OTA is depending on the activity of the peptidase enzyme. With this respect, several research groups showed that these carboxypeptidase enzymes tend to have high optimal temperatures (30°C or higher) which might hamper practical applications, observed with *Pediococcus parvulus* and several yeasts such as *Pfaffia rhodozyma* (Péteri et al., 2007; Patharajan et al., 2011; Abrunhosa et al., 2014). Other enzymes are also able to carry out this reaction: Deoxygenases, lipases, amidases, and several commercial proteases (Abrunhosa et al., 2006), have also been identified as carrying out this reaction. Although depending on the enzyme, intermediates can be different, the end product is always OTα.

Some interesting strains are highlighted here. *Trichosporon mycotoxinivorans* was demonstrated to deactivate OTA by conversion into the nontoxic OTα. Even more intriguingly, *T. mycotoxinivorans* was also able to decarboxylate ZEN (Molnar

et al., 2004; Vekiru et al., 2010). After 24 h, ZEN was degraded to carbon dioxide or into metabolites that neither showed fluorescence nor did absorb UV-light. Neither α- nor β-ZEL, other equally estrogenic metabolites of ZEN, could be detected. It is commercially applied as feed additive under the commercial name Biomin® MTV.

Phenylobacterium immobile (Wegst and Lingens, 1983) was also found to convert OTA to OTα through a dioxygenase step on the phenylalanine moiety, a dehydrogenation to catechol, a ring cleavage, and the final formation of OTα via a hydrolase.

UNEXPLORED WORLDS THAT MIGHT HARBOR VALUABLE MYCOTOXIN DEGRADING MICROORGANISMS

Targeting Carboxyl Esters

As stated above, fumonisins and acylated trichothecenes share carboxyl-esters which are involved in their toxicity. Detoxification of fumonisins is realized by removal of the tricarballylate side groups via carboxylesterases (EC 3.1.1.1). Similarly, acylated trichothecenes have several side groups where carboxylesterases could attack on the carboxyl group, as observed with carboxylesterases from rat liver microsomes (categorized as EC 3.1.1.1) degrading T-2 toxin into HT-2 toxin (Ohta et al., 1977; Johnsen et al., 1986). Carboxylesterases are multifunctional enzymes that catalyze the hydrolysis of substrates containing ester, amide, and thioester bonds with relatively broad substrate specificity (Bornscheuer, 2002) which is attributed to a large conformable active site that permits entry of numerous structurally diverse substrates. Microbial carboxylesterases have been reported in the degradation of pesticides; some hydrolyze pyrethroids and bind stoichiometrically to carbamates and organophosphates reviewed by Singh (2014). Several organisms have been isolated which degradative capacities of these compounds inferred by the expression of carboxylesterases, for which, bearing in mind their general broad substrate specificity, it might be worthwhile to screen for degradation of fumonisins and acylated trichothecenes. For example, broad-spectrum pyrethroid-hydrolyzing carboxylesterases were identified in the lambda-cyhalothrin degrading *Ochrobactrum anthropic* YZ-1 strain (Zhai et al., 2012) and *Bacillus* sp. DG-02, isolated from a pyrethroid-manufacturing wastewater treatment system (Chen et al., 2014). Similarly, an *Acinetobacter baumannii* strain was shown to degrade a wide range of organophosphorus compounds and evidence for a novel carboxylesterase in this strain was presented. Taking an environmental DNA (eDNA) isolation approach, Rashamuse et al. (2009) screened a microbial community to access novel carboxylesterases from environmental genomes: a carboxylesterase gene with 60% sequence identity to the gene from *Ralstonia eutropha* was identified, along with subsequent heterologous expression in *Escherichia coli* in a biologically active form. A similar approach might be taken to discover more mycotoxin-active carboxylases based on sequences of carboxylases present in *Sphingomonas* sp. ATCC 55552, *Exophiala* sp., or *Sphingopyxis* sp. MTA 144.

Targeting a Lactone Ring

The presence of a lactone moiety is shared by OTA, aflatoxins, and ZEN. Lactone chemicals are well-known as auto-regulators in both eukaryotic and prokaryotic cells. A well-known example is acyl homoserine lacton which is a quorum sensing molecule associated with biofilm formation. Because of the detrimental effects of biofilms in many industrial applications, high throughput research initiatives have been undertaken in the past and present in search for enzymes able to degrade these lactone molecules. These, often metagenomics, approaches result in the characterization of new and more efficient lactonase enzymes (Shimizu et al., 2001; Riaz et al., 2008; Schipper et al., 2009). The potential activities of these lactonases with respect to mycotoxins remains elusive but scientific fields studying biofilm issues might offer new microbial consortia ready to be explored for their mycotoxin degrading capacities.

Also targeted analyses can result in the characterization of new and efficient lactonase enzymes. In a screening assay for enzymes able to degrade bio-active lactones, a novel lactonohydrolase, an enzyme that catalyzes the hydrolysis of aldonate lactones to the corresponding aldonic acids, was purified from *Fusarium oxysporum* AKU 3702. The enzyme irreversibly hydrolyzes a broad spectrum of aromatic lactones, such as dihydrocoumarin and homogentisic-acid lactone (Shimizu et al., 1992; Kobayashi et al., 1998).

New insights for biodegradation of mycotoxins with estrogenic effects such as ZEN might come from studies on the microbial degradation of steroidal estrogens. Several strains have been isolated which are able to degrade the steroidal estrogen estrone (E1), also harboring a lactone ring (Yu et al., 2013), among which *Sphingomonas* sp. KC8 (Yu et al., 2007), *Bacillus subtilis* E2Y4 (Jiang et al., 2010), and several *Rhodococcus* sp. (Yoshimoto et al., 2004), remarkably all isolated from activated sludge. Also, cometabolic degradation of ethinyl estradiol (EE2) was obtained with nitrifying activated sludge (Vader et al., 2000). Therefore, activated sludge might prove to be a rich source of degradation potential for lactone-harboring mycotoxins.

Targeting an Epoxide Moiety

For trichothecenes, the epoxide moiety is an important chemical group associated with toxicity. Microbial transformation of epoxides was studied by Swaving and de Bont (1998) who demonstrated that two types of enzymes were responsible for detoxification of epoxides: glutathione transferases as a class of general detoxifying enzymes and epoxide hydrolases which are specific for detoxification of epoxides. Glutathione transferases (dependent on glutathione as cofactor) are mostly found in aerobic eukaryotes and prokaryotes, such as *E. coli* and *Rhodococcus* sp. which degrades a range of epoxides. Epoxide hydrolases are found in many microorganisms, like *Flavobacterium, Pseudomonas, Corynebacterium,* and *Stigmatella* species. Other enzymes can also convert an epoxide intermediate via a certain pathway (e.g., alpha-pinene oxide lyase from *Nocardia* sp. strain P18.3 and *Pseudomonas fluorescens* NCIMB 11671, styrene oxide isomerase of *Pseudomonas* species,

Xanthobacter 124X or *Exophilia jeanselmei,* or epoxyalkane-degrading enzyme in *Xanthobacter* Py2 (Swaving and de Bont, 1998). Broudiscou et al. (2007) proved that mono-and sesquiterpenes were degraded in the presence of mixed rumen microorganisms, corresponding with the isolation origin mostly found for microorganisms degrading trichothecenes. Ptaquiloside, also a sesquiterpene toxin, could be degraded by soil microorganisms (Engel et al., 2007) which can be a new source for biodegradation of trichothecenes.

Targeting Poly-Aromatic Ring Structures

White rot fungi are frequently found for degrading aflatoxins, such as *A. tabescens, P. sordida, P. ostreatus*, *T. versicolor,* and *Peniophora* sp. (Liu et al., 1998b; Motomura et al., 2003; Alberts et al., 2009; Wang et al., 2011; Das et al., 2014; Yehia, 2014). White rot fungi are well-known for their degrading capabilities of their natural substrate lignin and a broad spectrum of structurally diverse toxic environmental pollutants (e.g., munitions waste, pesticides, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, bleach plant effluent, synthetic dyes, synthetic polymers, and wood preservatives; Reddy, 1995; Pointing, 2001). Lignin peroxidases, manganese peroxidases and laccases are the major enzymes involved in lignin degradation based on oxidative mechanisms (Tuor et al., 1995). Laccases and manganese peroxidases of white rot fungi have been reported for degrading aflatoxins which possible can lead to different metabolites (Motomura et al., 2003; Wang et al., 2011). *Peniophora* sp. SCC0152, *P. ostreatus* St2-3, and several *Trametes* sp. strains demonstrated the degradation of Poly R-478 dye and AFB1 (Alberts et al., 2009). Next to white rot fungi, the genus *Rhodococcus* is also known to have promising degradation capability for xenobiotics (Martínková et al., 2009). Alberts et al. (2006) and Eshelli et al. (2015) suggested that degradation of AFB1 (polyaromatic compound) by a *Rhodococcus erythropolis* strain could be degraded in a similar way of degrading polyaromatic compounds of which their degradation occurs through a cascade of enzyme reactions (e.g., ring cleavage biphenyl dioxygenases, dihydrodiol dehydrogenases, and hydrolases). Degradation of a wide range of aromatic compounds results in a limited number of central intermediates (catechol, protocatechuate, gentisate) which are further degraded through central pathways for finally entering the citrate cycle (Martínková et al., 2009). In addition, *R. erythropolis* NI1 strain was found which was capable of degrading AFB1, ZEN, and T-2 toxin at the same time (Cserháti et al., 2013). Hence, various organisms have the potential for degrading multiple mycotoxins or other components, exemplified by. *Stenotrophomonas maltophilia, Stenotrophomonas* sp. NMO-3, and *Pseudomonas aeruginosa* which can degrade AFB1 and coumarin (Guan et al., 2008; Liang et al., 2008; Sangare et al., 2015), and *Mycobacterium fluoranthenivorans* FA4T which can degrade AFB1 and also grow on the polycyclic aromatic hydrocarbon fluoranthene (Hormisch et al., 2004).

Supporting the notion that microorganisms are able to metabolize structurally comparable chemicals from vastly different origins, a mixed enrichment culture capable of removing ZEN as sole carbon source, without the presence of derivatives, was obtained from soil collected at a coal gasification site, which are generally known to be associated with polycyclic aromatic hydrocarbon contamination. Removal of ZEN was enhanced in the presence of phenanthrene through enhanced microbial growth, indicating that organisms capable of using ZEN were also able to metabolize phenanthrene (Megharaj et al., 1997). Building further on this notion, cleaving the aromatic ring of ZEN by *A. niger* FS10 (Sun et al., 2014) and *Acinetobacter* sp. *SM04* (Yu et al., 2011a), for which no enzymes have been identified, might bear resemblance to the degradation of resorcinol (1,3-dihydroxybenzene) for which degradation is known by *P. putida* (Chapman Ribbons and Ribbons, 1976) and *Azotobacter vinelandii* (Groseclose and Ribbons, 1981).

Targeting a Carboxyl/Amide Moiety

Carboxypeptidase A and Y belong to the group of protease enzymes. Great interest in these enzymes comes from the field of wastewater treatments as these enzymes play a vital role in the extracellular catabolism of organic matter in activated sludge. In search of these enzymes, progressively more culture independent screening approaches are being employed as up to 90% of bacteria present in wastewater cannot be cultured and in this way a large reservoir of enzymes is overlooked. In matrices harboring a vast set of microorganisms that cannot be cultured, metagenomics analyses are often the solution to get an in depth insight into the complexity of these enzymes in a certain matrix. Pursuing this approach, a metagenomics analysis of waste water revealed a highly diverse phylogenetic diversity of carboxypeptidase gene sequences including previously undescribed types of carboxypeptidases which might be interesting to be applied for diverse biotechnological applications such as the remediation of OTA contaminated batches (Jin et al., 2014).

PERSPECTIVES

Although fumonisins, trichothecenes, ZEN, OTA, and aflatoxins comprise the major mycotoxin groups in food- and feed commodities, there are several other mycotoxins that were not addressed in present review because knowledge on biodegradation and detoxification is scarce. Cyclodepsipeptides such as beauvericin and enniatins are increasingly reported in many countries in several commodities. However, to our knowledge, no reports are available on their biodegradation and detoxification by microorganisms.The same accounts for ergot alkaloids such as lysergic acid, ergine, and ergopeptines. They occur widely but to date, only one paper has recently reported on a *R. erythropolis* isolate able to degrade these compounds (Thamhesl et al., 2015). Finally, for the *Penicllium expansum* mycotoxin patulin, recent papers report on biodegradation of this mycotoxin by *Pichia caribbica* (Cao et al., 2013), *Metschnikowia pulcherrima* (Reddy et al., 2011), *Kodameae ohmeri* (Dong et al., 2015), *Rhodosporidium* spp. (Castoria et al., 2011; Zhu et al., 2015), and *Saccharomyces cerevisiae* (Moss and Long, 2002). Nevertheless, for these emerging and also for the other mycotoxins, there is still a considerable need for concerted

research initiatives to identify new high-performance strains which can be implemented in practice.

Many surveys around the globe illustrate that mycotoxin contaminated batches of food and feed products often contain multiple both structurally related and non-related mycotoxins. An emerging approach to tackle this issue is biodegradation of mycotoxins by microorganisms. In our opinion an ideal biodegrading and detoxification agent should meet following features: (i) a fast and efficient degradation, (ii) of a broad spectrum of toxins, (iii) into non-toxic end products, (iv) by a non-pathogenic strain or consortium (v) under conditions that are relevant for the matrix in which the mycotoxin problem occurs. In order to do so, we urge researchers to look beyond the disappearance of the mother compound to rule out the creation of any *lesser evils*, and to *explore strange new worlds, seek out new organisms and new metabolic pathways*.

AUTHOR CONTRIBUTIONS

KA and LD conceived the idea and scope for the review. IV, KA, and LD all equally contributed to gathering and summarizing the literature, designing the tables and figures, and writing and editing of the paper.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fmicb.2016.00561

Figure 1 | Reduced toxicity of T-2 toxin by subsequent de-acylation.

Table 1 | Toxicity data on mycotoxins and their metabolites.

Table 2 | Toxicity of trichothecenes (from most potent to almost no effectiveness observed) (Thompson and Wannemacher, 1986).

REFERENCES

Abbas, H. K., Duke, S. O., and Tanaka, T. (1993a). Phytotoxicity of fumonisins and related-compounds. *J. Toxicol.-Toxin Rev.* 12, 225–251. doi: 10.3109/15569549309014408

Abbas, H. K., Gelderblom, W. C. A., Cawood, M. E., and Shier, W. T. (1993b). Biological-activities of fumonisins, mycotoxins from fusarium-moniliforme, in jimsonweed (*Datura-Stramonium* L) and mammalian-cell cultures. *Toxicon* 31, 345–353. doi: 10.1016/0041-0101(93)90152-9

Abbas, H. K., Tanaka, T., and Shier, W. T. (1995). Biological-activities of synthetic analogs of alternaria-alternata toxin (aal-toxin) and fumonisin in plant and mammalian-cell cultures. *Phytochemistry* 40, 1681–1689. doi: 10.1016/0031-9422(95)00470-R

Abrunhosa, L., Inês, A., Rodrigues, A. I., Guimaraes, A., Pereira, V. L., Parpot, P., et al. (2014). Biodegradation of ochratoxin A by *Pediococcus parvulus* isolated from Douro wines. *Int. J. Food Microbiol.* 188, 45–52. doi: 10.1016/j.ijfoodmicro.2014.07.019

Abrunhosa, L., Serra, R., and Venâncio, A. (2002). Biodegradation of ochratoxin A by fungi isolated from grapes. *J. Agric. Food Chem.* 50, 7493–7496. doi: 10.1021/jf025747i

Abrunhosa, L., Santos, L., and Venancio, A. (2006). Degradation of ochratoxin A by proteases and by a crude enzyme of Aspergillus niger. *Food Biotechnol.* 20, 231–242.

Adebo, O. A., Njobeh, P. B., Gbashi, S., Nwinyi, O. C., and Mavumengwana, V. (2015). Review on microbial degradation of aflatoxins. *Crit. Rev. Food Sci. Nutr.* doi: 10.1080/10408398.2015.1106440. [Epub ahead of print].

Alassane-Kpembi, I., Kolf-Clauw, M., Gauthier, T., Abrami, R., Abiola, F. A., Oswald, I. P., et al. (2013). New insights into mycotoxin mixtures: the toxicity of low doses of Type B trichothecenes on intestinal epithelial cells is synergistic. *Toxicol. Appl. Pharmacol.* 272, 191–198. doi: 10.1016/j.taap.2013.05.023

Alberts, J. F., Engelbrecht, Y., Steyn, P. S., Holzapfel, W., and van Zyl, W. (2006). Biological degradation of aflatoxin B-1 by *Rhodococcus erythropolis* cultures. *Int. J. Food Microbiol.* 109, 121–126. doi: 10.1016/j.ijfoodmicro.2006.01.019

Alberts, J. F., Gelderblom, W. C. A., Botha, A., and van Zyl, W. H. (2009). Degradation of aflatoxin B-1 by fungal laccase enzymes. *Int. J. Food Microbiol.* 135, 47–52. doi: 10.1016/j.ijfoodmicro.2009.07.022

Altalhi, A. D. (2007). Plasmid-mediated mycotoxin zearalenone in *Pseudomonas putida* ZEA-1. *Am. J. Biotechnol. Biochem.* 3, 150–158. doi: 10.3844/ajbbsp.2007.150.158

Altalhi, A. D., and El-Deeb, B. (2009). Localization of zearalenone detoxification gene(s) in pZEA-1 plasmid of *Pseudomonas putida* ZEA-1 and expressed in *Escherichia coli*. *J. Hazard. Mater.* 161, 1166–1172. doi: 10.1016/j.jhazmat.2008.04.068

Awad, W. A., Ghareeb, K., Bohm, J., and Zentek, J. (2010). Decontamination and detoxification strategies for the Fusarium mycotoxin deoxynivalenol in animal feed and the effectiveness of microbial biodegradation. *Food Addit. Contam. Part A-Chem. Anal. Control Expo. Risk Assess.* 27, 510–520. doi: 10.1080/19440040903571747

Babich, H., and Borenfreund, E. (1991). Cytotoxicity of T-2 toxin and its metabolites determined with the neutral red-cell viability assay. *Appl. Environ. Microbiol.* 57, 2101–2103.

Beardall, J. M., and Miller, J. D. (1994). "Diseases in humans with mycotoxins as possible causes," in *Mycotoxins in Grain: Compounds Other Than Aflatoxin*, eds J. D. Miller and H. L. Trenholm (St. Paul, MN: Eagan Press), 487–539.

Beeton, S., and Bull, A. T. (1989). Biotransformation and detoxification of T-2 toxin by soil and freshwater bacteria. *Appl. Environ. Microbiol.* 55, 190–197.

Bejaoui, H., Mathieu, F., Taillandier, P., and Lebrihi, A. (2006). Biodegradation of ochratoxin A by Aspergillus section Nigri species isolated from French grapes: a potential means of ochratoxin A decontamination in grape juices and musts. *Fems Microbiol. Lett.* 255, 203–208. doi: 10.1111/j.1574-6968.2005.00073.x

Benedetti, R., Nazzi, F., Locci, R., and Firrao, G. (2006). Degradation of fumonisin B1 by a bacterial strain isolated from soil. *Biodegradation* 17, 31–38. doi: 10.1007/s10532-005-2797-y

Bhat, R., Rai, R. V., and Karim, A. A. (2010). Mycotoxins in food and feed: present status and future concerns. *Compr. Rev. Food Sci. Food Safety* 9, 57–81. doi: 10.1111/j.1541-4337.2009.00094.x

Binder, E. M. (2007). Managing the risk of mycotoxins in modern feed production. *Anim. Feed Sci. Technol.* 133, 149–166. doi: 10.1016/j.anifeedsci.2006.08.008

Binder, E. M., and Binder, J. (2004). *Strain of Eubacterium that Detoxifies Trichothecenes*. US Patent 6, 794–175. (Original patent owner: Erber Aktiengesell Schaft). Washington, DC: United States Patent and Trademark Office.

Blackwell, B. A., Gilliam, J. T., Savard, M. E., Miller, J. D., and Duvick, J. P. (1999). Oxidative deamination of hydrolyzed fumonisin B(1) (AP(1)) by cultures of Exophiala spinifera. *Nat. Toxins* 7, 31–38.

Bornscheuer, U. T. (2002). Microbial carboxyl esterases: classification, properties and application in biocatalysis. *FEMS Microbiol. Rev.* 26, 73–81. doi: 10.1111/j.1574-6976.2002.tb00599.x

Bové, F. J. (1970). *The Story of Ergot*. Basel: S. Karger.

Broudiscou, L. P., Cornu, A., and Rouzeau, A. (2007). *in vitro* degradation of 10 mono- and sesquiterpenes of plant origin by caprine rumen micro-organisms. *J. Sci. Food Agric.* 87, 1653–1658. doi: 10.1002/jsfa.2863

Bruinink, A., and Sidler, C. (1997). The neurotoxic effects of ochratoxin-A are reduced by protein binding but are not affected by I-phenylalanine. *Toxicol. Appl. Pharmacol.* 146, 173–179. doi: 10.1006/taap.1997.8229

Bullerman, L. B., and Bianchini, A. (2007). Stability of mycotoxins during food processing. *Int. J. Food Microbiol.* 119, 140–146. doi: 10.1016/j.ijfoodmicro.2007.07.035

Camilo, S. B., Ono, C. J., Ueno, Y., and Hirooka, E. Y. (2000). Anti-Fusarium moniliforme activity and fumonisin biodegradation by corn and silage microflora. *Braz. Arch. Biol. Technol.* 43, 159–164. doi: 10.1590/S1516-89132000000200004

Cao, J., Zhang, H., Yang, Q., and Ren, R. (2013). Efficacy of *Pichia caribbica* in controlling blue mold rot and patulin degradation in apples. *Int. J. Food Microbiol.* 162, 167–173. doi: 10.1016/j.ijfoodmicro.2013.01.007

Castells, M., Ramos, A. J., Sanchis, V., and Marín, S. (2007). Distribution of total aflatoxins in milled fractions of hulled rice. *J. Agric. Food Chem.* 55, 2760–2764. doi: 10.1021/jf063252d

Castoria, R., Mannina, L., Durán-Patrón, R., Maffei, F., Sobolev, A. P., De Felice, D. V., et al. (2011). Conversion of the mycotoxin patulin to the less toxic desoxypatulinic acid by the biocontrol yeast rhodosporidium kratochvilovae strain LS11. *J. Agric. Food Chem.* 59, 11571–11578. doi: 10.1021/jf203098v

Chang, X., Wu, Z., Wu, S., Dai, Y., and Sun, C. (2015). Degradation of ochratoxin A by *Bacillus amyloliquefaciens* ASAG1. *Food Addit. Contam. Part A-Chem. Anal. Control Expos. Risk Assess.* 32, 564–571. doi: 10.1080/19440049.2014.991948

Chapman, P. J., and Ribbons, D. W. (1976). Metabolism of resorcinylic compounds by bacteria - alternative pathways for resorcinol catabolism in *Pseudomonas-Putida*. *J. Bacteriol.* 125, 985–998.

Cheli, F., Pinotti, L., Rossi, L., and Dell'orto, V. (2013). Effect of milling procedures on mycotoxin distribution in wheat fractions: a review. *LWT-Food Sci. Technol.* 54, 307–314. doi: 10.1016/j.lwt.2013.05.040

Chen, S., Chang, C., Deng, Y., An, S., Dong, Y. H., Zhou, J., et al. (2014). Fenpropathrin biodegradation pathway in bacillus sp DG-02 and its potential for bioremediation of pyrethroid-contaminated soils. *J. Agric. Food Chem.* 62, 2147–2157. doi: 10.1021/jf404908j

Ciegler, A., Lillehoj, E. B., Peterson, R. E., and Hall, H. H. (1966). Microbial detoxification of aflatoxin. *Appl. Microbiol.* 14, 934–939.

Clarke, R., Connolly, L., Frizzell, C., and Elliott, C. T. (2014). Cytotoxic assessment of the regulated, co-existing mycotoxins aflatoxin B1, fumonisin B1 and ochratoxin, in single, binary and tertiary mixtures. *Toxicon* 90, 70–81. doi: 10.1016/j.toxicon.2014.07.019

Creppy, E. E. (2002). Update of survey, regulation and toxic effects of mycotoxins in Europe. *Toxicol. Lett.* 127, 19–28. doi: 10.1016/S0378-4274(01)00479-9

Cserháti, M., Kriszt, B., Krifaton, C., Szoboszlay, S., Hahn, J., Toth, S., et al. (2013). Mycotoxin-degradation profile of Rhodococcus strains. *Int. J. Food Microbiol.* 166, 176–185. doi: 10.1016/j.ijfoodmicro.2013.06.002

Cundliffe, E., Cannon, M., and Davies, J. (1974). Mechanism of inhibition of eukaryotic protein-synthesis by trichothecene fungal toxins. *Proc. Natl. Acad. Sci. U.S.A.* 71, 30–34. doi: 10.1073/pnas.71.1.30

Cundliffe, E., and Davies, J. E. (1977). Inhibition of initiation, elongation, and termination of eukaryotic protein-synthesis by trichothecene fungal toxins. *Antimicrob. Agents Chemother.* 11, 491–499. doi: 10.1128/AAC.11.3.491

Da Rocha, M. E. B., Freire, F. D. O., Maia, F. B. F., Guedes, M. I. F., and Rondina, D. (2014). Mycotoxins and their effects on human and animal health. *Food Control* 36, 159–165. doi: 10.1016/j.foodcont.2013.08.021

Das, A., Bhattacharya, S., Palaniswamy, M., and Angayarkanni, J. (2014). Biodegradation of aflatoxin B1 in contaminated rice straw by *Pleurotus ostreatus* MTCC 142 and *Pleurotus ostreatus* GHBBF10 in the presence of metal salts and surfactants. *World J. Microbiol. Biotechnol.* 30, 2315–2324. doi: 10.1007/s11274-014-1657-5

De Bellis, P., Tristezza, M., Haidukowski, M., Fanelli, F., Sisto, A., Mulè, G., et al. (2015). Biodegradation of ochratoxin a by bacterial strains isolated from vineyard soils. *Toxins* 7, 5079–5093. doi: 10.3390/toxins7124864

de Felice, D. V., Solfrizzo, M., De Curtis, F., Lima, G., Visconti, A., and Castoria, R. (2008). Strains of aureobasidium pullulans can lower ochratoxin A contamination in wine grapes. *Phytopathology* 98, 1261–1270. doi: 10.1094/PHYTO-98-12-1261

De Mil, T., Devreese, M., Broekaert, N., Fraeyman, S., De Backer, P., and Croubels, S. (2015). *in vitro* adsorption and *in vivo* pharmacokinetic interaction between doxycycline and frequently used mycotoxin binders in broiler chickens. *J. Agric. Food Chem.* 63, 4370–4375. doi: 10.1021/acs.jafc.5b00832

Devreese, M., De Backer, P., and Croubels, S. (2013). Different methods to counteract mycotoxin production and its impact on animal health. *Vlaams Diergeneeskundig Tijdschrift* 82, 181–190.

Dobritzsch, D., Wang, H., Schneider, G., and Yu, S. (2014). Structural and functional characterization of ochratoxinase, a novel mycotoxin-degrading enzyme. *Biochem. J.* 462, 441–452. doi: 10.1042/BJ20140382

Dong, X., Jiang, W., Li, C., Ma, N., Xu, Y., and Meng, X. (2015). Patulin biodegradation by marine yeast *Kodameae ohmeri*. *Food Addit. Contam. Part A-Chem. Anal. Control Expos. Risk Assess.* 32, 352–360. doi: 10.1080/19440049.2015.1007090

Dridi, F., Marrakchi, M., Gargouri, M., Saulnier, J., Jaffrezic-Renault, N., and Lagarde, F. (2015). Comparison of carboxypeptidase Y and thermolysin for ochratoxin A electrochemical biosensing. *Anal. Methods* 7, 8954–8960. doi: 10.1039/C5AY01905B

Duvick, J., Maddox, J., and Gilliam, J. (2003). *Compositions and Methods for Fumonisin Detoxification*. US Patent No. 6538177 (Original patent owner: Pioneer Hi-Bred International, Inc.). Charlotte, NC: United States Patent and Trademark Office.

Duvick, J., Rood, T., Maddox, J., and Gilliam, J. (1998a). "Detoxification of mycotoxins in planta as a strategy for improving grain quality and disease resistance: identification of fumonisin-degrading microbes from maize," in *Molecular Genetics of Host-Specific Toxins in Plant Disease,* eds K. Kohmoto and O. Yoder (Dordrecht: Kluwer Academic Publishers), 369–381.

Duvick, J., Rood, T., and Wang, N. (1998b). *Fumonisin Detoxification Enzymes*. US Patent No. 5716820 (Original patent owner: Pioneer Hi-Bred International, Inc.). United States Patent and Trademark Office.

Eaton, D. L., and Groopman, J. D. (1994). *The Toxicology of Aflatoxins: Human Health, Veterinary, and Agricultural Significance*. San Diego, CA: Academic Press.

Ehrlich, K. C., and Daigle, K. W. (1987). Protein-Synthesis Inhibition by 8-Oxo-12,13-Epoxytrichothecenes. *Biochim. Biophys. Acta* 923, 206–213. doi: 10.1016/0304-4165(87)90005-5

El-sharkawy, S., and Abul-hajj, Y. J. (1988). Microbial cleavage of zearalenone. *Xenobiotica* 18, 365–371. doi: 10.3109/00498258809041672

El-sharkawy, S. H., and Abul-hajj, Y. J. (1988). Microbial transformation of zearalenone.2. *Reduction, hydroxylation, and methylation products. J. Org. Chem.* 53, 515–519. doi: 10.1021/jo00238a008

Engel, P., Brandt, K. K., Rasmussen, L. H., Ovesen, R. G., and Sorensen, J. (2007). Microbial degradation and impact of Bracken toxin ptaquiloside on microbial communities in soil. *Chemosphere* 67, 202–209. doi: 10.1016/j.chemosphere.2006.08.025

Engelhardt, G. (2002). Degradation of ochratoxin a and b by the white rot fungus *Pleurotus ostreatus*. *Mycol. Res.* 18, 37–43. doi: 10.1007/bf02946138

Engler, K. H., Coker, R. D., and Evans, I. H. (1999). A colorimetric technique for detecting trichothecenes and assessing relative potencies. *Appl. Environ. Microbiol.* 65, 1854–1857.

Eriksen, G. S., and Pettersson, H. (2004). Toxicological evaluation of trichothecenes in animal feed. *Anim. Feed Sci. Technol.* 114, 205–239. doi: 10.1016/j.anifeedsci.2003.08.008

Eriksen, G. S., Pettersson, H., Johnsen, K., and Lindberg, J. E. (2002). Transformation of trichothecenes in ileal digesta and faeces from pigs. *Arch. Tierernahr.* 56, 263–274. doi: 10.1080/00039420214343

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

Eshelli, M., Harvey, L., Edrada-Ebel, R., and Mcneil, B. (2015). Metabolomics of the bio-degradation process of aflatoxin B1 by actinomycetes at an initial pH of 6.0. *Toxins* 7, 439–456. doi: 10.3390/toxins7020439

Fandohan, P., Ahouansou, R., Houssou, P., Hell, K., Marasas, W. F. O., and Wingfield, M. J. (2006). Impact of mechanical shelling and dehulling on Fusarium infection and fumonisin contamination in maize. *Food Addit. Contam.* 23, 415–421. doi: 10.1080/02652030500442516

Fandohan, P., Zoumenou, D., Hounhouigan, D. J., Marasas, W. F. O., Wingfield, M. J., and Hell, K. (2005). Fate of aflatoxins and fumonisins during the processing of maize into food products in Benin. *Int. J. Food Microbiol.* 98, 249–259. doi: 10.1016/j.ijfoodmicro.2004.07.007

Ferenczi, S., Cserháti, M., Krifaton, C., Szoboszlay, S., Kukolya, J., Szoke, Z., et al. (2014). A new ochratoxin A biodegradation strategy using *Cupriavidus basilensis* or16 strain. *PLoS ONE* 9:e109817. doi: 10.1371/journal.pone.0109817

Fuchs, E., Binder, E., Heidler, D., and Krska, R. (2000). Characterisation of metabolites after the microbial degradation of A- and B-trichothecenes by BBSH 797. *Mycotoxin Res.* 16, 66–69. doi: 10.1007/BF02942984

Fuchs, E., Binder, E. M., Heidler, D., and Krska, R. (2002). Structural characterization of metabolites after the microbial degradation of type A trichothecenes by the bacterial strain BBSH 797. *Food Addit. Contam.* 19, 379–386. doi: 10.1080/02652030110091154

Fuchs, S., Sontag, G., Stidl, R., Ehrlich, V., Kundi, M., and Knasmüeller, S. (2008). Detoxification of patulin and ochratoxin A, two abundant mycotoxins, by lactic acid bacteria. *Food Chem. Toxicol.* 46, 1398–1407. doi: 10.1016/j.fct.2007.10.008

Gelderblom, W. C. A., Jaskiewicz, K., Marasas, W. F. O., Thiel, P. G., Horak, R. M., Vleggaar, R., et al. (1988). Fumonisins - novel mycotoxins with cancer-promoting activity produced by *Fusarium-moniliforme*. *Appl. Environ. Microbiol.* 54, 1806–1811.

Gerding, J., Cramer, B., and Humpf, H. U. (2014). Determination of mycotoxin exposure in Germany using an LC-MS/MS multibiomarker approach. *Mol. Nutr. Food Res.* 58, 2358–2368. doi: 10.1002/mnfr.201400406

Groseclose, E. E., and Ribbons, D. W. (1981). Metabolism of resorcinylic compounds by bacteria - new pathway for resorcinol catabolism in *Azotobacter-vinelandii*. *J. Bacteriol.* 146, 460–466.

Grove, M. D., Plattner, R. D., and Peterson, R. E. (1984). Detection of aflatoxin D1 in ammoniated corn by mass-spectrometry mass-spectrometry. *Appl. Environ. Microbiol.* 48, 887–889.

Guan, S., He, J. W., Young, J. C., Zhu, H. H., Li, X. Z., Ji, C., et al. (2009). Transformation of trichothecene mycotoxins by microorganisms from fish digesta. *Aquaculture* 290, 290–295. doi: 10.1016/j.aquaculture.2009.02.037

Guan, S., Ji, C., Zhou, T., Li, J. X., Ma, Q., and Niu, T. (2008). Aflatoxin B-1 degradation by *Stenotrophomonas maltophilia* and other microbes selected using coumarin medium. *Int. J. Mol. Sci.* 9, 1489–1503. doi: 10.3390/ijms9081489

Guengerich, F. P., Johnson, W. W., Ueng, Y. F., Yamazaki, H., and Shimada, T. (1996). Involvement of cytochrome P450, glutathione S-transferase, and epoxide hydrolase in the metabolism of aflatoxin B-1 and relevance to risk of human liver cancer. *Environ. Health Perspect.* 104, 557–562.

Hahn, I., Kunz-Vekiru, E., Twaruzek, M., Grajewski, J., Krska, R., and Berthiller, F. (2015). Aerobic and anaerobic *in vitro* testing of feed additives claiming to detoxify deoxynivalenol and zearalenone. *Food Addit. Contam. Part A-Chem. Anal. Control Expos. Risk Assess.* 32, 922–933. doi: 10.1080/19440049.2015.1023741

Hartinger, D., Heinl, S., Grabherr, R., Schatzmayr, G., and Moll, W. D. (2009). Heterologous expression of genes from the fumonisin degradation gene cluster of Sphingomonas spp. MTA144 and activity of the catabolic enzymes. *New Biotechnol.* 25, S132–S133. doi: 10.1016/j.nbt.2009.06.444

Hathout, A. S., and Aly, S. E. (2014). Biological detoxification of mycotoxins: a review. *Ann. Microbiol.* 64, 905–919. doi: 10.1007/s13213-014-0899-7

He, J. W. (2015). *Detoxification of Deoxynivalenol by a Soil Bacterium Devosia mutans 17-2-E-8*. Ph.D. thesis, The University of Guelph.

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

Heinl, S., Hartinger, D., Moll, W. D., Schatzmayr, G., and Grabherr, R. (2009). Identification of a fumonisin B1 degrading gene cluster in Sphingomonas spp. MTA144. *New Biotechnol.* 25, S61–S62. doi: 10.1016/j.nbt.2009.06.290

Heinl, S., Hartinger, D., Thamhesl, M., Schatzmayr, G., Moll, W. D., and Grabherr, R. (2011). An aminotransferase from bacterium ATCC 55552 deaminates hydrolyzed fumonisin B-1. *Biodegradation* 22, 25–30. doi: 10.1007/s10532-010-9371-y

Heinl, S., Hartinger, D., Thamhesl, M., Vekiru, E., Krska, R., Schatzmayr, G., et al. (2010). Degradation of fumonisin B-1 by the consecutive action of two bacterial enzymes. *J. Biotechnol.* 145, 120–129. doi: 10.1016/j.jbiotec.2009.11.004

Hormisch, D., Brost, I., Kohring, G. W., Giffhorn, E., Kroppenstedt, R. M., Stackebrandt, E., et al. (2004). Mycobacterium fluoranthenivorans sp nov., a fluoranthene and aflatoxin B-1 degrading bacterium from contaminated soil of a former coal gas plant. *Syst. Appl. Microbiol.* 27, 653–660. doi: 10.1078/0723202042369866

Hussein, H. S., and Brasel, J. M. (2001). Toxicity, metabolism, and impact of mycotoxins on humans and animals. *Toxicology* 167, 101–134. doi: 10.1016/S0300-483X(01)00471-1

Huwig, A., Freimund, S., Kappeli, O., and Dutler, H. (2001). Mycotoxin detoxication of animal feed by different adsorbents. *Toxicol. Lett.* 122, 179–188. doi: 10.1016/S0378-4274(01)00360-5

Hwang, C. A., and Draughon, F. A. (1994). Degradation of ochratoxin-a by *Acinetobacter-calcoaceticus*. *J. Food Prot.* 57, 410–414.

IARC (2002). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Aflatoxins*. Lyon: IARC Press.

Ikunaga, Y., Sato, I., Grond, S., Numaziri, N., Yoshida, S., Yamaya, H., et al. (2011). Nocardioides sp. strain WSN05-2, isolated from a wheat field, degrades deoxynivalenol, producing the novel intermediate 3-epi-deoxynivalenol. *Appl. Microbiol. Biotechnol.* 89, 419–427. doi: 10.1007/s00253-010-2857-z

Jard, G., Liboz, T., Mathieu, F., Guyonvarc'h, A., and Lebrihi, A. (2011). Review of mycotoxin reduction in food and feed: from prevention in the field to detoxification by adsorption or transformation. *Food Addit. Contam. Part A-Chem. Anal. Control Expos. Risk Assess.* 28, 1590–1609. doi: 10.1080/19440049.2011.595377

Jiang, L. Y., Yang, J., and Chen, J. M. (2010). Isolation and characteristics of 17 beta-estradiol-degrading Bacillus spp. strains from activated sludge. *Biodegradation* 21, 729–736. doi: 10.1007/s10532-010-9338-z

Jin, H., Li, B., Peng, X., and Chen, L. M. (2014). Metagenomic analyses reveal phylogenetic diversity of carboxypeptidase gene sequences in activated sludge of a wastewater treatment plant in Shanghai, China. *Ann. Microbiol.* 64, 689–697. doi: 10.1007/s13213-013-0704-z

Johnsen, H., Odden, E., Lie, O., Johnsen, B. A., and Fonnum, F. (1986). Metabolism of T-2 toxin by rat-liver carboxylesterase. *Biochem. Pharmacol.* 35, 1469–1473. doi: 10.1016/0006-2952(86)90111-5

Kakeya, H., Takahashi-Ando, N., Kimura, M., Onose, R., Yamaguchi, I., and Osada, H. (2002). Biotransformation of the mycotoxin, zearalenone, to a non-estrogenic compound by a fungal strain of Clonostachys sp. *Biosci. Biotechnol. Biochem.* 66, 2723–2726. doi: 10.1271/bbb.66.2723

Karabulut, S., Paytakov, G., and Leszczynski, J. (2014). Reduction of aflatoxin B1 to aflatoxicol: a comprehensive DFT study provides clues to its toxicity. *J. Sci. Food Agric.* 94, 3134–3140. doi: 10.1002/jsfa.6663

Kaushik, G. (2015). Effect of processing on mycotoxin content in grains. *Crit. Rev. Food Sci. Nutr.* 55, 1672–1683. doi: 10.1080/10408398.2012.701254

Khatibi, P. A., Berger, G., Wilson, J., Brooks, W. S., McMaster, N., Griffey, C. A., et al. (2014). A comparison of two milling strategies to reduce the mycotoxin deoxynivalenol in barley. *J. Agric. Food Chem.* 62, 4204–4213. doi: 10.1021/jf501208x

Kimura, M., Tokai, T., Takahashi-Ando, N., Ohsato, S., and Fujimura, M. (2007). Molecular and genetic studies of Fusarium trichothecene biosynthesis: pathways, genes, and evolution. *Biosci. Biotechnol. Biochem.* 71, 2105–2123. doi: 10.1271/bbb.70183

Klaric, M. S., Rašic, D., and Peraica, M. (2013). Deleterious effects of mycotoxin combinations involving ochratoxin A. *Toxins* 5, 1965–1987. doi: 10.3390/toxins5111965

Kobayashi, M., Shinohara, M., Sakoh, C., Kataoka, M., and Shimizu, S. (1998). Lactone-ring-cleaving enzyme: genetic analysis, novel RNA editing, and evolutionary implications. *Proc. Natl. Acad. Sci. U.S.A.* 95, 12787–12792. doi: 10.1073/pnas.95.22.12787

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

Krifaton, C., Kriszt, B., Risa, A., Szoboszlay, S., Cserháti, M., Harkai, P., et al. (2013). Application of a yeast estrogen reporter system for screening zearalenone degrading microbes. *J. Hazard. Mater.* 244, 429–435. doi: 10.1016/j.jhazmat.2012.11.063

Krifaton, C., Kriszt, B., Szoboszlay, S., Cserháti, M., Szucs, A., and Kukolya, J. (2011). Analysis of aflatoxin-B1-degrading microbes by use of a combined toxicity-profiling method. *Mutat. Res.* 726, 1–7. doi: 10.1016/j.mrgentox.2011.07.011

Kriszt, R., Krifaton, C., Szoboszlay, S., Cserháti, M., Kriszt, B., Kukolya, J., et al. (2012). A new zearalenone biodegradation strategy using non-pathogenic rhodococcus pyridinivorans K408 strain. *PLoS ONE* 7: e43608. doi: 10.1371/journal.pone.0043608

Larkin, M. J., Kulakov, L. A., and Allen, C. C. R. (2005). Biodegradation and Rhodococcus - masters of catabolic versatility. *Curr. Opin. Biotechnol.* 16, 282–290. doi: 10.1016/j.copbio.2005.04.007

Lee, L. S., Dunn, J. J., DeLucca, A. J., and Ciegler, A. (1981). Role of lactone ring of aflatoxin-B1 in toxicity and mutagenicity. *Experientia* 37, 16–17. doi: 10.1007/BF01965543

Li, Y., Wang, Z., Beier, R. C., Shen, J. Z., De Smet, D., De Saeger, S., et al. (2011). T-2 toxin, a trichothecene mycotoxin: review of toxicity, metabolism, and analytical methods. *J. Agric. Food Chem.* 59, 3441–3453. doi: 10.1021/jf200767q

Liang, Z., Li, J., He, Y., G, S., Wang, N., Ji, C., et al. (2008). AFB1 bio-degradation by a new strain - *Stenotrophomonas*. sp. *Agric. Sci. China* 7, 1433–1437. doi: 10.1016/S1671-2927(08)60399-5

Liu, D. L., Ma, L., Gu, L. Q., Liang, R., Yao, D. S., and Chen, W. Q. (1998a). Armillariella tabescen enzymatic detoxification of aflatoxin B-1 - Part III. *Immobilized enzymatic detoxification. Enzyme Eng.* 864, 592–599. doi: 10.1111/j.1749-6632.1998.tb10387.x

Liu, D. L., Yao, D. S., Liang, R., Ma, L., Cheng, W. Q., and Gu, L. Q. (1998b). Detoxification of aflatoxin B-1 by enzymes isolated from *Armillariella tabescens*. *Food Chem. Toxicol.* 36, 563–574. doi: 10.1016/S0278-6915(98)00017-9

Liu, D. L., Yao, D. S., Liang, Y. Q., Zhou, T. H., Song, Y. P., Zhao, L., et al. (2001). Production, purification, and characterization of an intracellular aflatoxin-detoxifizyme from *Armillariella tabescens* (E-20). *Food Chem. Toxicol.* 39, 461–466. doi: 10.1016/S0278-6915(00)00161-7

Manahan, S. E. (2002). *Toxicological Chemistry and Biochemistry*. Boca Raton, FL: CRC Press.

Mann, R., and Rehm, H. J. (1976). Degradation products from aflatoxin-B1 by corynebacterium-rubrum, aspergillus-niger, trichoderma-viride and mucor-ambiguus. (Boca Raton: USA) *Eur. J. Appl. Microbiol.* 2, 297–306. doi: 10.1007/BF01278613

Marroquín-Cardona, A. G., Johnson, N. M., Phillips, T. D., and Hayes, A. W. (2014). Mycotoxins in a changing global environment - a review. *Food Chem. Toxicol.* 69, 220–230. doi: 10.1016/j.fct.2014.04.025

Martínková, L., Uhnáková, B., Pátek, M., Nesvera, J., and Kren, V. (2009). Biodegradation potential of the genus Rhodococcus. *Environ. Int.* 35, 162–177. doi: 10.1016/j.envint.2008.07.018

Matsushima, T., Okamoto, E., Miyagawa, E., Matsui, Y., Shimizu, H., and Asano, K. (1996). Deacetylation of diacetoxyscirpenol to 15-acetoxyscirpenol by rumen bacteria. *J. Gen. Appl. Microbiol.* 42, 225–234. doi: 10.2323/jgam.42.225

Matthies, I., Woerfel, G., and Karlovsky, P. (2001). Induction of a zearalenone degrading enzyme caused by the substrate and its derivatives. *Mycotoxin Res.* 17(Suppl. 1), 28–31. doi: 10.1007/BF03036706

Matumba, L., Van Poucke, C., Ediage, E. N., Jacobs, B., and De Saeger, S. (2015). Effectiveness of hand sorting, flotation/washing, dehulling and combinations thereof on the decontamination of mycotoxin-contaminated white maize. *Food Addit. Contam. Part A-Chem. Anal. Control Expos. Risk Assess.* 32, 960–969. doi: 10.1080/19440049.2015.1029535

McCormick, S. P. (2013). Microbial detoxification of mycotoxins. *J. Chem. Ecol.* 39, 907–918. doi: 10.1007/s10886-013-0321-0

McCormick, S. P., Price, N. P. J., and Kurtzman, C. P. (2012). Glucosylation and other biotransformations of t-2 toxin by yeasts of the trichomonascus clade. *Appl. Environ. Microbiol.* 78, 8694–8702. doi: 10.1128/AEM.02391-12

McCormick, S. P., Stanley, A. M., Stover, N. A., and Alexander, N. J. (2011). Trichothecenes: from simple to complex mycotoxins. *Toxins* 3, 802–814. doi: 10.3390/toxins3070802

Megharaj, M., Garthwaite, I., and Thiele, J. H. (1997). Total biodegradation of the oestrogenic mycotoxin zearalenone by a bacterial culture. *Lett. Appl. Microbiol.* 24, 329–333. doi: 10.1046/j.1472-765X.1997.00053.x

Méndez-Albores, A., Arámbula-Villa, G., Loarea-Piña, M. G. F., Castaño-Tostado, E., and Moreno-Martínez, E. (2005). Safety and efficacy evaluation of aqueous citric acid to degrade B-aflatoxins in maize. *Food Chem. Toxicol.* 43, 233–238. doi: 10.1016/j.fct.2004.09.009

Merrill, A. H., Vanechten, G., Wang, E., and Sandhoff, K. (1993a). Fumonisin-B(1) inhibits sphingosine (sphinganine) N-acyltransferase and *de-novo* sphingolipid biosynthesis in cultured neurons *in-situ*. *J. Biol. Chem.* 268, 27299–27306.

Merrill, A. H. Jr., Wang, E., Gilchrist, D. G., and Riley, R. T. (1993b). Fumonisins and other inhibitors of *de-novo* sphingolipid biosynthesis. *Adv. Lipid Res.* 26, 215–234.

Moll, W.-D., Hartinger, D., Griebler, K., Binder, E. M., and Schatzmayr, D. (2014). *Method for the Production of an Additive for the Enzymatic Decomposition of Mycotoxins, Additive, and Use Thereof*. US Patent No. 8703460 (Original patent owner: Erber Aktiengesell Schaft). Washington, DC: United States Patent and Trademark Office.

Molnar, O., Schatzmayr, G., Fuchs, E., and Prillinger, H. (2004). *Trichosporon mycotoxinivorans* sp nov., a new yeast species useful in biological detoxification of various mycotoxins. *Syst. Appl. Microbiol.* 27, 661–671. doi: 10.1078/0723202042369947

Moss, M. O., and Long, M. T. (2002). Fate of patulin in the presence of the yeast *Saccharomyces cerevisiae*. *Food Addit. Contam.* 19, 387–399. doi: 10.1080/02652030110091163

Motomura, M., Toyomasu, T., Mizuno, K., and Shinozawa, T. (2003). Purification and characterization of an aflatoxin degradation enzyme from *Pleurotus ostreatus*. *Microbiol. Res.* 158, 237–242. doi: 10.1078/0944-5013-00199

Norred, W. P., Plattner, R. D., Dombrink-kurtzman, M. A., Meredith, F. I., and Riley, R. T. (1997). Mycotoxin-induced elevation of free sphingoid bases in precision-cut rat liver slices: specificity of the response and structure-activity relationships. *Toxicol. Appl. Pharmacol.* 147, 63–70. doi: 10.1006/taap.1997.8272

Norred, W. P., Voss, K. A., Bacon, C. W., and Riley, R. T. (1991). Effectiveness of ammonia treatment in detoxification of fumonisin contaminated corn. *Food Chem. Toxicol.* 29, 815–819. doi: 10.1016/0278-6915(91)90108-J

Ohta, M., Ishii, K., and Ueno, Y. (1977). Metabolism of trichothecene mycotoxins.1. microsomal deacetylation of t-2 toxin in animal-tissues. *J. Biochem.* 82, 1591–1598.

Patharajan, S., Reddy, K. R. N., Karthikeyan, V., Spadaro, D., Lore, A., Gullino, M. L., et al. (2011). Potential of yeast antagonists on *in vitro* biodegradation of ochratoxin A. *Food Control* 22, 290–296. doi: 10.1016/j.foodcont.2010.07.024

Peraica, M., Radic, B., Lucic, A., and Pavlovic, M. (1999). Toxic effects of mycotoxins in humans. *Bull. World Health Org.* 77, 754–766.

Petchkongkaew, A., Taillandier, P., Gasaluck, P., and Lebrihi, A. (2008). Isolation of *Bacillus* spp. from Thai fermented soybean (thua-nao): screening for aflatoxin B-1 and ochratoxin A detoxification. *J. Appl. Microbiol.* 104, 1495–1502. doi: 10.1111/j.1365-2672.2007.03700.x

Péteri, Z., Téren, J., Vágvölgyi, C., and Varga, J. (2007). Ochratoxin degradation and adsorption caused by astaxanthin-producing yeasts. *Food Microbiol.* 24, 205–210. doi: 10.1016/j.fm.2006.06.003

Pfohl-Leszkowicz, A., and Manderville, R. A. (2007). Ochratoxin A: an overview on toxicity and carcinogenicity in animals and humans. *Mol. Nutr. Food Res.* 51, 1192–1192. doi: 10.1002/mnfr.200790020

Pointing, S. B. (2001). Feasibility of bioremediation by white-rot fungi. *Appl. Microbiol. Biotechnol.* 57, 20–33. doi: 10.1007/s002530100745

Popiel, D., Koczyk, G., Dawidziuk, A., Gromadzka, K., Blaszczyk, L., and Chelkowski, J. (2014). Zearalenone lactonohydrolase activity in Hypocreales and its evolutionary relationships within the epoxide hydrolase subset of a/b-hydrolases. *BMC Microbiol.* 14:82. doi: 10.1186/1471-2180-14-82

Rafiqul, I. (2012). *Isolation, Characterization and Genome Sequencing of a Soil-Borne Citrobacter Freundii Strain Capable of Detoxifying Trichothecene Mycotoxins*. Ph.D. thesis, The University of Guelph, Guelph.

Ramos, A. J., Finkgremmels, J., and Hernandez, E. (1996). Prevention of toxic effects of mycotoxins by means of nonnutritive adsorbent compounds. *J. Food Prot.* 59, 631–641.

Rashamuse, K., Ronneburg, T., Hennessy, F., Visser, D., Van Heerden, E., Piater, L., et al. (2009). Discovery of a novel carboxylesterase through functional screening of a pre-enriched environmental library. *J. Appl. Microbiol.* 106, 1532–1539. doi: 10.1111/j.1365-2672.2008.04114.x

Reddy, C. A. (1995). The potential for white-rot fungi in the treatment of pollutants. *Curr. Opin. Biotechnol.* 6, 320–328. doi: 10.1016/0958-1669(95)80054-9

Reddy, K. R. N., Spadaro, D., Gullino, M. L., and Garibaldi, A. (2011). Potential of two *Metschnikowia pulcherrima* (yeast) strains for *in vitro* biodegradation of patulin. *J. Food Prot.* 74, 154–156. doi: 10.4315/0362-028X.JFP-10-331

Riaz, K., Elmerich, C., Moreira, D., Raffoux, A., Dessaux, Y., and Faure, D. (2008). A metagenomic analysis of soil bacteria extends the diversity of quorum-quenching lactonases. *Environ. Microbiol.* 10, 560–570. doi: 10.1111/j.1462-2920.2007.01475.x

Richard, J. L. (2007). Some major mycotoxins and their mycotoxicoses - an overview. *Int. J. Food Microbiol.* 119, 3–10. doi: 10.1016/j.ijfoodmicro.2007.07.019

Rios, G., Pinson-Gadais, L., Abecassis, J., Zakhia-Rozis, N., and Lullien-Pellerin, V. (2009). Assessment of dehulling efficiency to reduce deoxynivalenol and Fusarium level in durum wheat grains. *J. Cereal Sci.* 49, 387–392. doi: 10.1016/j.jcs.2009.01.003

Rocha, O., Ansari, K., and Doohan, F. M. (2005). Effects of trichothecene mycotoxins on eukaryotic cells: a review. *Food Addit. Contam. Part A-Chem. Anal. Control Expos. Risk Assess.* 22, 369–378. doi: 10.1080/02652030500058403

Rodriguez, H., Reveron, I., Doria, F., Costantini, A., De Las Rivas, B., Munoz, R., et al. (2011). Degradation of ochratoxin a by brevibacterium species. *J. Agric. Food Chem.* 59, 10755–10760. doi: 10.1021/jf203061p

Samuel, M. S., Aiko, V., Panda, P., and Metha, A. (2013). Aflatoxin B1 occurance, biosynthesis and its degradation. *J. Pure Appl. Microbiol.* 7, 965–971.

Samuel, M. S., Sivaramakrishna, A., and Mehta, A. (2014). Degradation and detoxification of aflatoxin B1 by *Pseudomonas putida*. *Int. Biodeterior. Biodegradation* 86, 202–209. doi: 10.1016/j.ibiod.2013.08.026

Sangare, L., Zhao, Y. J., Folly, Y. M. E., Chang, J. H., Li, J. H., Selvaraj, J. N., et al. (2015). Aflatoxin B-1 degradation by a pseudomonas strain. *Toxins* 7, 3538–3539. doi: 10.3390/toxins7093538

Sato, I., Ito, M., Ishizaka, M., Ikunaga, Y., Sato, Y., Yoshida, S., et al. (2012). Thirteen novel deoxynivalenol-degrading bacteria are classified within two genera with distinct degradation mechanisms. *FEMS Microbiol. Lett.* 327, 110–117. doi: 10.1111/j.1574-6968.2011.02461.x

Schatzmayr, G., Heidler, D., Fuchs, E., Mohnl, M., Täubel, M., Loibner, A. P., et al. (2003). Investigation of different yeast strains for the detoxification of ochratoxin A. *Mycotoxin Res.* 19, 124–128. doi: 10.1007/BF02942950

Schiff, P. L. (2006). Ergot and its alkaloids. *Am. J. Pharm. Educ.* 70, 98–107. doi: 10.5688/aj700598

Schipper, C., Hornung, C., Bijtenhoorn, P., Quitschau, M., Grond, S., and Streit, W. R. (2009). Metagenome-derived clones encoding two novel lactonase family proteins involved in biofilm inhibition in *Pseudomonas aeruginosa*. *Appl. Environ. Microbiol.* 75, 224–233. doi: 10.1128/AEM.01389-08

Scudamore, K. A., Baillie, H., Patel, S., and Edwards, S. G. (2007). Occurrence and fate of Fusarium mycotoxins during commercial processing of oats in the UK. *Food Addit. Contam.* 24, 1374–1385. doi: 10.1080/02652030701509972

Shier, W. T., Shier, A. C., Xie, W., and Mirocha, C. J. (2001). Structure-activity relationships for human estrogenic activity in zearalenone mycotoxins. *Toxicon* 39, 1435–1438. doi: 10.1016/S0041-0101(00)00259-2

Shima, J., Takase, S., Takahashi, Y., Iwai, Y., Fujimoto, H., Yamazaki, M., et al. (1997). Novel detoxification of the trichothecene mycotoxin deoxynivalenol by a soil bacterium isolated by enrichment culture. *Appl. Environ. Microbiol.* 63, 3825–3830.

Shimizu, S., Kataoka, M., Honda, K., and Sakamoto, K. (2001). Lactone-ring-cleaving enzymes of microorganisms: their diversity and applications. *J. Biotechnol.* 92, 187–194. doi: 10.1016/S0168-1656(01)00359-5

Shimizu, S., Kataoka, M., Shimizu, K., Hirakata, M., Sakamoto, K., and Yamada, H. (1992). Purification and characterization of a novel lactonohydrolase, catalyzing the hydrolysis of aldonate lactones and aromatic lactones, from fusarium-oxysporum. *Eur. J. Biochem.* 209, 383–390. doi: 10.1111/j.1432-1033.1992.tb17300.x

Singh, B. (2014). Review on microbial carboxylesterase: general properties and role in organophosphate pesticides degradation. *Biochem. Mol. Biol.* 2, 1–6. doi: 10.12966/bmb.03.01.2014

Soriano, J. M., González, L., and Catala, A. I. (2005). Mechanism of action of sphingolipids and their metabolites in the toxicity of fumonisin B1. *Progr. Lipid Res.* 44, 345–356. doi: 10.1016/j.plipres.2005.09.001

Stander, M. A., Bornscheuer, U. T., Henke, E., and Steyn, P. S. (2000). Screening of commercial hydrolases for the degradation of ochratoxin A. *J. Agric. Food Chem.* 48, 5736–5739. doi: 10.1021/jf000413j

Stander, M. A., Steyn, P. S., Van Der Westhuizen, F. H., and Payne, B. E. (2001). A kinetic study into the hydrolysis of the ochratoxins and analogues by carboxypeptidase A. *Chem. Res. Toxicol.* 14, 302–304. doi: 10.1021/tx000221i

Storm, I. M. L. D., Rasmussen, R. R., and Rasmussen, P. H. (2014). Occurrence of pre- and post-harvest mycotoxins and other secondary metabolites in Danish maize silage. *Toxins* 6, 2256–2269. doi: 10.3390/toxins6082256

Sudakin, D. L. (2003). Trichothecenes in the environment: relevance to human health. *Toxicol. Lett.* 143, 97–107. doi: 10.1016/S0378-4274(03)00116-4

Sun, X., He, X., Xue, K., Li, Y., Xu, D., and Qian, H. (2014). Biological detoxification of zearalenone by *Aspergillus niger* strain FS10. *Food Chem. Toxicol.* 72, 76–82. doi: 10.1016/j.fct.2014.06.021

Swanson, S. P., Nicoletti, J., Rood, H. D., Buck, W. B., Cote, L. M., and Yoshizawa, T. (1987). Metabolism of 3 trichothecene mycotoxins, t-2 toxin, diacetoxyscirpenol and deoxynivalenol, by bovine rumen microorganisms. *J. Chromatogr.* 414, 335–342. doi: 10.1016/0378-4347(87)80058-0

Swaving, J., and de Bont, J. A. M. (1998). Microbial transformation of epoxides. *Enzyme Microb. Technol.* 22, 19–26. doi: 10.1016/S0141-0229(97)00097-5

Takahashi-Ando, N., Ohsato, S., Shibata, T., Hamamoto, H., Yamaguchi, I., and Kimura, M. (2004). Metabolism of zearalenone by genetically modified organisms expressing the detoxification gene from *Clonostachys rosea*. *Appl. Environ. Microbiol.* 70, 3239–3245. doi: 10.1128/AEM.70.6.3239-3245.2004

Tan, H., Hu, Y., He, J., Wu, L., Liao, F., Luo, B., et al. (2014). Zearalenone degradation by two Pseudomonas strains from soil. *Mycotoxin Res.* 30, 191–196. doi: 10.1007/s12550-014-0199-x

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

Täubel, M. (2005). *Isolierung und Charakterisierung von Mikroorganismen zur biologischen Inaktivierung von Fumonisinen*. Doctoral thesis, University of Natural Resources and Applied Life Sciences, Vienna, Austria.

Tejada-Castañeda, Z. I., Avila-Gonzalez, E., Casaubon-Huguenin, M. T., Cervantes-Olivares, R. A., Vásquez-Peláez, C., Hernandez-Baumgarten, E. M., et al. (2008). Biodetoxification of aflatoxin-contaminated chick feed. *Poult. Sci.* 87, 1569–1576. doi: 10.3382/ps.2007-00304

Teniola, O. D., Addo, P. A., Brost, I. M., Färber, P., Jany, K. D., Alberts, J. F., et al. (2005). Degradation of aflatoxin B-1 by cell-free extracts of *Rhodococcus erythropolis* and *Mycobacterium fluoranthenivorans* sp. nov DSM44556(T). *Int. J. Food Microbiol.* 105, 111–117. doi: 10.1016/j.ijfoodmicro.2005.05.004

Thamhesl, M., Apfelthaler, E., Schwartz-Zimmermann, H. E., Kunz-Vekiru, E., Krska, R., and Kneifel, W. et al. (2015). Rhodococcus erythropolis MTHt3 biotransforms ergopeptines to lysergic acid. *Bmc Microbiol.* 15:73. doi: 10.1186/s12866-015-0407-7

Thompson, W. L., and Wannemacher, R. W. (1986). Structure-function-relationships of 12,13-epoxytrichothecene mycotoxins in cell-culture - comparison to whole animal lethality. *Toxicon* 24, 985–994. doi: 10.1016/0041-0101(86)90004-8

Tintelnot, T., Tegtmeyer, F., and Klotz, M. (2011). Trichosporon mycotoxinovorans -a sword of Damocles for patients with cystic fibrosis. *Mycoses* 54, 373. doi: 10.1111/j.1439-0507.2011.02066.x

Tinyiro, S. E., Wokadala, C., Xu, D., and Yao, W. (2011). Adsorption and degradation of zearalenone by bacillus strains. *Folia Microbiol.* 56, 321–327. doi: 10.1007/s12223-011-0047-8

Tsuge, T., Harimoto, Y., Akimitsu, K., Ohtani, K., Kodama, M., Akagi, Y., et al. (2013). Host-selective toxins produced by the plant pathogenic fungus *Alternaria alternata*. *FEMS Microbiol. Rev.* 37, 44–66. doi: 10.1111/j.1574-6976.2012.00350.x

Tuor, U., Winterhalter, K., and Fiechter, A. (1995). Enzymes of white-rot fungi involved in lignin degradation and ecological determinants for wood decay. *J. Biotechnol.* 41, 1–17. doi: 10.1016/0168-1656(95)00042-O

Ueno, Y., Nakayama, K., Ishii, K., Tashiro, F., Minoda, Y., Omori, T., et al. (1983). Metabolism of T-2-Toxin in Curtobacterium Sp Strain-114-2. *Appl. Environ. Microbiol.* 46, 120–127.

Vader, J. S., van Ginkel, C. G., Sperling, F. M. G. M., de Jong, J., De Boer, W., De Graaf, J. S., et al. (2000). Degradation of ethinyl estradiol by nitrifying activated sludge. *Chemosphere* 41, 1239–1243. doi: 10.1016/S0045-6535(99)00556-1

van der Westhuizen, L., Shephard, G. S., Rheeder, J. P., Burger, H. M., Gelderblom, W. C. A., Wild, C. P., et al. (2011). Optimising sorting and washing of home-grown maize to reduce fumonisin contamination under laboratory-controlled conditions. *Food Control* 22, 396–400. doi: 10.1016/j.foodcont.2010.09.009

Vanheule, A., De Boevre, M., Audenaert, K., Beaert, B., De Saeger, S., and Haesaert, G. (2014). Occurence of Fusarium species and their associated mycotoxins in unprocessed cereals, food and feed products in Belgium. *Int. J. Food Microbiol.* 181, 28–36. doi: 10.1016/j.ijfoodmicro.2014.04.012

Varga, J., Péteri, Z., Tábori, K., Téren, J., and Vagvolgyi, C. (2005). Degradation of ochratoxin A and other mycotoxins by Rhizopus isolates. *Int. J. Food Microbiol.* 99, 321–328. doi: 10.1016/j.ijfoodmicro.2004.10.034

Vekiru, E., Hametner, C., Mitterbauer, R., Rechthaler, J., Adam, G., Schatzmayr, G., et al. (2010). Cleavage of zearalenone by *Trichosporon mycotoxinivorans* to a novel nonestrogenic metabolite. *Appl. Environ. Microbiol.* 76, 2353–2359. doi: 10.1128/AEM.01438-09

Völkl, A., Vogler, B., Schollenberger, M., and Karlovsky, P. (2004). Microbial detoxification of mycotoxin deoxynivalenol. *J. Basic Microbiol.* 44, 147–156. doi: 10.1002/jobm.200310353

Voss, K. A., Bacon, C. W., Meredith, F. I., and Norred, W. P. (1996a). Comparative subchronic toxicity studies of nixtamalized and water-extracted Fusarium moniliforme culture material. *Food Chem. Toxicol.* 34, 623–632. doi: 10.1016/0278-6915(96)00024-5

Voss, K. A., Riley, R. T., Bacon, C. W., Chamberlain, W. J., and Norred, W. P. (1996b). Subchronic toxic effects of Fusarium moniliforme and fumonisin B1 in rats and mice. *Nat. Toxins* 4, 16–23. doi: 10.1002/19960401NT3

Voss, K. A., Smith, G. W., and Haschek, W. M. (2007). Fumonisins: toxicokinetics, mechanism of action and toxicity. *Anim. Feed Sci. Technol.* 137, 299–325. doi: 10.1016/j.anifeedsci.2007.06.007

Wang, J. Q., Ogata, M., Hirai, H., and Kawagishi, H. (2011). Detoxification of aflatoxin B-1 by manganese peroxidase from the white-rot fungus *Phanerochaete sordida* YK-624. *FEMS Microbiol. Lett.* 314, 164–169. doi: 10.1111/j.1574-6968.2010.02158.x

Wegst, W., and Lingens, F. (1983). Bacterial-degradation of ochratoxin-A. *FEMS Microbiol. Lett.* 17, 341–344. doi: 10.1111/j.1574-6968.1983.tb00433.x

Westlake, K., Mackie, R. I., and Dutton, M. F. (1987). T-2 toxin metabolism by ruminal bacteria and its effect on their growth. *Appl. Environ. Microbiol.* 53, 587–592.

Wogan, G. N., Newberne, P. M., and Edwards, G. S. (1971). Structure-activity relationships in toxicity and carcinogenicity of aflatoxins and analogs. *Cancer Res.* 31, 1936–1942.

Wong, J. J., and Hsieh, D. P. H. (1976). Mutagenicity of aflatoxins related to their metabolism and carcinogenic potential. *Proc. Natl. Acad. Sci. U.S.A.* 73, 2241–2244. doi: 10.1073/pnas.73.7.2241

Wu, Q., Jezkova, A., Yuan, Z., Pavlikova, L., Dohnal, V., and Kuca, K. (2009). Biological degradation of aflatoxins. *Drug Metab. Rev.* 41, 1–7. doi: 10.1080/03602530802563850

Xiao, H., Madhyastha, S., Marquardt, R. R., Li, S., Vodela, J. K., Frohlich, A. A., et al. (1996). Toxicity of ochratoxin A, its opened lactone form and several of its analogs: structure-activity relationships. *Toxicol. Appl. Pharmacol.* 137, 182–192. doi: 10.1006/taap.1996.0071

Yehia, R. S. (2014). Aflatoxin detoxification by manganese peroxidase purified from *Pleurotus ostreatus*. *Braz. J. Microbiol.* 45, 127–133. doi: 10.1590/S1517-83822014005000026

Yiannikouris, A., Bertin, G., and Jouany, J. P. (2006). Study of the adsorption capacity of *Saccharomyces cerevisiae* cell wall components toward mycotoxins and the chemical mechanisms invoked. *Mycotoxin Factbook* 347–361. doi: 10.3920/978-90-8686-587-1

Yoshimoto, T., Nagai, F., Fujimoto, J., Watanabe, K., Mizukoshi, H., Makino, T., et al. (2004). Degradation of estrogens by Rhodococcus zopfii and Rhodococcus equi isolates from activated sludge in wastewater treatment plants. *Appl. Environ. Microbiol.* 70, 5283–5289. doi: 10.1128/AEM.70.9.5283-5289.2004

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

Yu, C. P., Deeb, R. A., and Chu, K. H. (2013). Microbial degradation of steroidal estrogens. *Chemosphere* 91, 1225–1235. doi: 10.1016/j.chemosphere.2013.01.112

Yu, C. P., Roh, H., and Chu, K. H. (2007). 17 beta-estradiol-degrading bacteria isolated from activated sludge. *Environ. Sci. Technol.* 41, 486–492. doi: 10.1021/es060923f

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

Yu, Y. S., Qiu, L. P., Wu, H., Tang, Y. Q., Lai, F. R., and Yu, Y. G. (2011a). Oxidation of zearalenone by extracellular enzymes from Acinetobacter sp SM04 into smaller estrogenic products. *World J. Microbiol. Biotechnol.* 27, 2675–2681. doi: 10.1007/s11274-011-0741-3

Yu, Y. S., Qiu, L., Wu, H., Tang, Y., Yu, Y., Li, X., et al. (2011b). Degradation of zearalenone by the extracellular extracts of Acinetobacter sp SM04 liquid cultures. *Biodegradation* 22, 613–622. doi: 10.1007/s10532-010-9435-z

Zhai, Y., Li, K., Song, J. L., Shi, Y. H., and Yan, Y. C. (2012). Molecular cloning, purification and biochemical characterization of a novel pyrethroid-hydrolyzing carboxylesterase gene from *Ochrobactrum anthropi* YZ-1. *J. Hazard. Mater.* 221, 206–212. doi: 10.1016/j.jhazmat.2012.04.031

Zhou, T., Gong, J., Young, J. C., Yu, H., Li, X. Z., Zhu, H., et al. (2007). *"Microorganisms isolated from chicken gut can effectively detoxify DON and other trichothecene mycotoxins," in 26th Centralia Swine Research Update* (Ontario).

Zhou, T., He, J., and Gong, J. (2008). Microbial transformation of trichothecene mycotoxins. *World Mycotoxin J.* 1, 23–30. doi: 10.3920/WMJ2008.x003

Zhu, R., Feussner, K., Wu, T., Yan, F., Karlovsky, P., and Zheng, X. (2015). Detoxification of mycotoxin patulin by the yeast Rhodosporidium paludigenum. *Food Chem.* 179, 1–5. doi: 10.1016/j.foodchem.2015.01.066

Zinedine, A., Soriano, J. M., Moltó, J. C., and Mañes, J. (2007). Review on the toxicity, occurrence, metabolism, detoxification, regulations and intake of zearalenone: an oestrogenic mycotoxin. *Food Chem. Toxicol.* 45, 1–18. doi: 10.1016/j.fct.2006.07.030

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.