Animal Nutrition 2 (2016) 127–133

Contents lists available at ScienceDirect

Animal Nutrition

journal homepage: http://www.keaipublishing.com/en/journals/aninu/

Review Article

Review on biological degradation of mycotoxins

Cheng Ji, Yu Fan, Lihong Zhao*

State Key Laboratory of Animal Nutrition, College of Animal Science and Technology, China Agricultural University, Beijing 100193, China

ARTICLE INFO

Article history:
Received 24 February 2016
Received in revised form
3 July 2016
Accepted 13 July 2016
Available online 19 July 2016

Keywords:
Biological degradation
Mycotoxins
Aflatoxins
Zearalenone
Deoxynivalenol

ABSTRACT

The worldwide contamination of feeds and foods with mycotoxins is a significant problem. Mycotoxins pose huge health threat to animals and humans. As well, mycotoxins bring enormous economic losses in food industry and animal husbandry annually. Thus, strategies to eliminate or inactivate mycotoxins in food and feed are urgently needed. Traditional physical and chemical methods have some limitations such as limited efficacy, safety issues, losses in the nutritional value and the palatability of feeds, as well as the expensive equipment required to implement these techniques. Biological degradation of mycotoxins has shown promise because it works under mild, environmentally friendly conditions. Aflatoxin (AF), zearalenone (ZEA) and deoxynivalenol (DON) are considered the most economically important mycotoxins in terms of their high prevalence and significant negative effects on animal performance. Therefore, this review will comprehensively describe the biological degradation of AF, ZEA and DON by microorganisms (including fungi and bacteria) and specific enzymes isolated from microbial systems that can convert mycotoxins with varied efficiency to non- or less toxic products. Finally, some strategies and advices on existing difficulties of biodegradation research are also briefly proposed in this paper.

© 2016, Chinese Association of Animal Science and Veterinary Medicine. Production and hosting by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Mycotoxins are a large group of secondary metabolic products from fungi, or molds, which pose serious risks for human and animal health. Fungal growth and mycotoxin production may occur in the field and/or during storage, under suitable temperature and humidity conditions (Bryden, 2012). Mycotoxin contamination occurs widely in feedstuffs of plant origin, especially in cereals, fruits, hazelnuts, almonds, seeds, fodder, and other agricultural feed or food intended for animal or human consumption (Guan et al., 2011;Wu et al., 2013, 2014, 2015a,b). It is also worth noting that human exposure to mycotoxins may be caused by not only consumption of plant-derived foods contaminated with toxins, but also the carry-over of mycotoxins and their metabolites in animal products, such as animal tissues, milk and eggs (CAST, 2002). Moreover, mycotoxins lead to huge economic losses annually, including loss of human and animal life, loss of livestock production, loss of forage crops and feeds, and so on (Mohamed, 2011).

It is well known that not all molds are toxigenic and not all secondary metabolites from molds are toxic (Mohamed, 2011). Currently, more than 300 mycotoxins have been identified, and scientific attention is focused mainly on the mycotoxins that have proven carcinogenic and/or toxic. Thus, aflatoxins (AF), zearalenone (ZEA) and deoxynivalenol (DON) elicit great public health concerns due to their high prevalence, and their teratogenic, carcinogenic, mutagenic and immunosuppressive effects (Miazzo et al., 2000; Oueslati et al., 2012).

Aflatoxins, produced mainly by *Aspergillus flavus* and *Aspergillus parasiticus* (Wogan and Pong, 1970), are recognized as the most hazardous mycotoxins. The liver is the primary target organ for AF. Long-term intake of feeds contaminated with AF results in negative effects on the liver, such as hepatic cell and tissue injury, as well as gross and microscopic abnormalities (Williams et al., 2011; Gholami-Ahangaran et al., 2016). In classical epidemiology, researchers revealed the relationship between AF exposure and high prevalence of human liver cancer in various areas of Asia and Africa (Pitt, 2000). Zearalenone, produced by several *Fusarium* species, in particular *Fusarium graminearum* and *Fusarium culmorum*,

* Corresponding author.
E-mail address: zhaolihongcau@cau.edu.cn (L. Zhao).

Peer review under responsibility of Chinese Association of Animal Science and Veterinary Medicine.

Production and Hosting by Elsevier on behalf of KeAi

http://dx.doi.org/10.1016/j.aninu.2016.07.003
2405-6545/© 2016, Chinese Association of Animal Science and Veterinary Medicine. Production and hosting by Elsevier B.V. on behalf of KeAi Communications Co., Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

competitively binds to estrogen receptors causing reproductive disorders and estrogenic dysfunction in humans and animals (Borutova et al., 2012; Schoevers et al., 2012). Swine have been shown to be very sensitive to ZEA. Zearalenone may lead to swelling of the vulva and mammary glands, vulvovaginitis, vaginal and/or rectal prolapse, disrupted conception, abortion and infertility in swine (Stoev, 2015). Deoxynivalenol, also produced mainly by *Fusarium* species, is one of the most frequently detected trichothecene contaminants in grains (Mishra et al., 2013). The ingestion of low or moderate dose of DON causes nausea, diarrhea, gastrointestinal tract lesions, decreased nutritional efficiency, and weight loss in animals. Higher dose of DON induces vomiting and feed refusal with severe reduction in weight, severe damage in the hematopoietic systems and immune dysregulation (Maresca, 2013; Wu et al., 2015a,b). Swine is the animal species most severely affected by DON.

In an eight-year study on occurrence of mycotoxins in feed and feed raw materials worldwide, a total of 56,672 analysis were conducted on 17,316 samples for the determination of AF, ZEA, DON, fumonisins and ochratoxin A (Streit et al., 2013). The results showed that 72% of the samples tested positive for at least one mycotoxin, and 38% were found to be co-contaminated with multi-mycotoxins. In a recent paper, Li et al. (2014) reported that DON, aflatoxin B_1 (AFB_1) and ZEA were detected at percentages of 97%, 70% and 100%, respectively, in feeding ingredients and complete feeds obtained from swine farms in the Beijing region of China. The co-occurrence of several mycotoxins occurs frequently because of the ability of a given mold species to produce several kinds of mycotoxins in one type of food ingredient. Besides, the complete feeds, made from different contaminated ingredients or raw materials, may also have several types of mycotoxins. Co-contaminated feeds probably lead to adverse effects even though the concentration of the individual mycotoxin does not surpass legal maximum limit (Streit et al., 2013).

Numerous traditional physical and chemical strategies for the elimination or inactivation of mycotoxins have been reported in the literature (Stoev, 2013). Nevertheless, these methods have some limitations concerning safety issues, losses in the nutritional value and the palatability of feeds, coupled with limited efficacy and cost implication. In recent years, using mycotoxin-adsorbing agents, to bind mycotoxins in gastrointestinal tract of animals and then decrease their bioavailability and toxicities, shows a promising potential in feed industrial applications. However, there are various kinds of adsorption agents and their efficacy in preventing mycotoxicosis varies (Mohamed, 2011). Adsorption agents are very useful to prevent aflatoxicosis, but are not very effective for other mycotoxins (Stoev, 2013). Therefore, seeking for an effective, specific, feasible and environmentally sound decontamination technology is in a great demand. The biological detoxification of mycotoxins, using microorganisms and/or enzymes to degrade mycotoxins to non- or less toxic compounds, can be a choice of such technology (Taylor and Draughon, 2001). This review is mainly focused on the biological detoxification of AF, ZEA and DON.

2. Biological degradation of aflatoxins

2.1. Fungi

A number of fungal species have shown an ability to degrade AF (Mishra and Das, 2003; Wu et al., 2009). Fungi *Aspergillus* species, including *A. parasiticus*, *Aspergillus white*, *A. flavus* and *Aspergillus niger*, were reported early to be able to degrade AF. Doyle and Marth (1978) found that the mycelial blend of *A. parasiticus* NRRL 2999 could degrade AFB_1 and AFG_1 in the reaction mixture, and the degradation rates of AFB_1 and AFG_1 proportionally increased with the increase of the initial aflatoxin concentration or the size of mycelia inoculum. Then, Huynh et al. (1984) extracted a crude mycelial protein, which could detoxify AFB_1, from a 16-day-old culture of *A. parasiticus* using $(NH_4)_2SO_4$ at 80% to 100% precipitation. In their study, the main breakdown product of AFB_1 was isolated, and was confirmed to be non-fluorescent, non-mutagenic, and non-toxic for ducklings. The result showed that the dialyzed mycelial protein destructed AF by degradation of the cyclopentenone moiety, principally the lactone ring, via infrared spectral analysis of the main breakdown product. Mann and Rehm (1976) reported another species of *Aspergillus*, *A. niger*, was able to convert AFB_1 into aflatoxicol (AFL). Zhang et al. (2014) screened a strain of *A. niger* (ND-1) that could degrade 58.2% of AFB_1 after 48 h of fermentation. The degradation activity of *A. niger* was significantly stronger in culture supernatant than cells and cell extracts, and affected by heat treatment, temperature, pH, and metal ions, indicating that the degradation reaction is enzymatic and this process mainly occurs in the extracellular environment. Mishra and Das (2003) have reviewed other *Aspergillus* species possessing capability to biodegrade AF.

Nakazato et al. (1985) investigated the effect of incubation period on the conversion of AFB_1 into AFL by *Eurotium rubrum*. The accumulation of AFL in the cultures began on the 2nd day, rapidly increased between the 6th day and the 8th day, and then gradually decreased toward the 15th day, the end of the incubation period. *Phoma* sp. not only prevented AF formation but also degraded preformed AF (Shantha, 1999). When the reaction mixture containing cell-free extracts of *Phoma* sp. and AFB_1 was incubated for 5 days without and with heating in boiling water for 10 min, significant degradation was observed in both the cases. This suggested a possible role for a heat stable enzyme in the degradation. Reports on other fungi detoxifying AF have been reviewed by Wu et al. (2009). Briefly, *Penicillium raistrickii* NRRL 2038 could convert AFB_1 to a compound that is similar to AFB_2 (Ciegler et al., 1966). *Dactylium dendroides* (NRRL 2575), *Mucor griseocyanus* (NRRL 3359), *Mucor alternans* (NRRL 3358), *Absidia repens* (NRRL 1336), *Helminthosporium sativum* (NRRL 3356), *Muco rambiguous* (I.M.M. 115), and *Trichoderma viride* (ATCC 13233) could transform AFB_1 to a new fluorescent-blue compound AFR_0, namely AFL, through a carbonyl reduction in the cyclopentane ring (Detroy and Hesselti., 1969; Mann and Rehm, 1976). The conversion of AFG_1 to AFB_3 (parasiticol) by *Rhizopus stolonifer* (NRRL 1477), *Rhizopus arrhizus* (NRRL 2585) and *Rhizopus oryzae* (NRRL 395) was studied by Cole and Kirksey (1971). Cole et al. (1972) revealed that two fluorescent metabolites of AFB_1 accumulated during degradation by *R. stolonifer*, *R. arrhizus* and *R. oryzae*, were identified as hydroxylated stereo isomers derived from reduction of the ketone function on the cyclopentane ring of AFB_1. *Rhizopus oligosporus* [F0216] was able to inhibit synthesis of AFB_1 or to degrade AFB_1 (Kusumaningtyas et al., 2006). Some white rot fungi exhibiting high laccase activity, e.g., *Peniophora* and *Pleurotus ostreatus*, also had the potential to degrade AFB_1 (Alberts et al., 2009).

2.2. Bacteria

Aflatoxins can be metabolized by certain species of *Actinomycetales*, such as *Nocardia corynebacterioides* (formerly classified as *Flavobacterium aurantiacum*), *Nocardia asteroids*, *Corynebacterium rubrum*, *Rhodococcus erythropolis*, *Mycobacterium fluoranthenivorans*, and *Mycobacterium smegmatis*. *C. rubrum* eliminated more than 99% of the added AFB_1 (1.48 μg/mL) in a liquid culture after 4 days (Mann and Rehm, 1976). Kong et al. (2012) adopted Plackett–Burman design and central composite design to screen the key factors and identify the optimal conditions for degradation of AFB_1 by *R. erythropolis*, and eventually the AFB_1

degradation efficiency was increased from 28.7% to 95.8%. Taylor et al. (2010) identified nine *M. smegmatis* enzymes that utilized the deazaflavin cofactor $F_{420}H_2$ to catalyze the reduction of the α, β-unsaturatedester moiety of AF, activating the molecules for spontaneous hydrolysis and detoxification. These enzymes belonged to two $F_{420}H_2$ dependent reductase (FDR-A and -B) families. In another work of this team (Lapalikar et al., 2012), they indicated that the FDR-A enzymes had up to 100 times more activity than the FDR-B enzymes, meanwhile, they tested another ten FDR-A enzymes from other *Actinomycetales* and found that nine of them can also reduce AFB_1 and AFG_1. This suggested that AF reducing activity might be widespread in this family of enzymes and the order of *Actinomycetales*, as the family of enzymes was itself widespread in the *Actinomycetales*. More studies on other *Actinomycetales* for elimination of AF have been discussed in the reviews by Bata and Lásztity (1999), Mishra and Das (2003), and Wu et al. (2009).

It was reported that *Pseudomonas aeruginosa* N17-1 could degrade AFB_1, AFB_2 and AFM_1 by 82.8%, 46.8% and 31.9% after incubation in Nutrient Broth medium at 37°C for 72 h, respectively (Sangare et al., 2014). Some *Bacillus* sp. also displayed aflatoxin reduction activity, such as *Bacillus subtilis* (Farzaneh et al., 2012), *Bacillus licheniformis* (Petchkongkaew et al., 2008), and so on.

In the attempt to develop the technology for detoxifying AF with microorganisms, our research team has intensively studied bacterial isolates capable of biodegrading AF. Guan et al. (2008) used cumarin as the sole carbon source to screen the bacterial isolates with AFB_1 reduction activity. And they found that *Stenotrophomonas maltophilia* 35-3, obtained from tapir feces, could reduce AFB_1 by 82.5% after incubation in the liquid medium at 37°C for 72 h. Its culture supernatant was able to degrade AFB_1 effectively, whereas the viable cells and cell extracts were far less effective. And treatments with proteinase K, proteinase K plus sodium dodecyl sulfate (SDS) and heating significantly reduced or eradicated the degradation activity of the culture supernatant, indicating that the degradation of AFB_1 by *S. maltophilia* 35-3 was enzymatic. *Myxococcus fulvus* ANSM068, isolated from deer feces, was also able to transform AFB_1 (Guan et al., 2010). Liquid chromatography mass spectrometry and infrared analysis indicated that AFB_1 was transformed to a structurally different compound, and the lactone ring on the AFB_1 molecule was modified by the culture supernatant. In addition, Gao et al. (2011) isolated a strain of *B. subtilis* ANSB060 from fish gut showing a strong ability to detoxify AF, and percentages of AFB_1, AFM_1, and AFG_1 degradation were 81.5%, 60%, and 80.7%, respectively. Also, ANSB060 showed antimicrobial activities against *Escherichia coli*, *Salmonella typhimurium*, *Staphylococcus aureus* and resistance to the simulated gut environments. Moreover, the protective effects of supplementation of *B. subtilis* ANSB060 in the aflatoxin-contaminated diets on layers and broilers have been verified well in the studies *in vivo* (Ma et al., 2012; Fan et al., 2013, 2015).

2.3. Enzyme

A kind of pure laccase enzyme from *Trametes versicolor* (1 U/mL) could degrade AFB_1 by 87.34% after incubation for 72 h (Alberts et al., 2009). Zeinvand-Lorestani et al. (2015) found that the optimal enzymatic reaction occurred in 0.1 mol/L of citrate buffer containing 20% dimethyl sulfoxide (DMSO) at 35°C, a pH of 4.5, and a laccase activity of 30 U/mL; and after two days, 67% of AFB_1 was removed. Manganese peroxidase (MnP) from the white-rot fungus *Phanerochaete sordida* YK-624 could first oxidize AFB_1 to AFB_1-8, 9-epoxide and then hydrolyze to AFB_1-8, 9-dihydrodiol (Wang et al., 2011). Similarly, Yehia (2014) purified MnP from white rot edible mushroom *P. ostreatus*, with the final enzyme activity achieving 81 U/mL and specific activity achieving 78 U/mg. The highest detoxification power (90%) was observed after incubation for 48 h at 1.5 U/mL enzyme activities. As well, The MnP-cDNA encoding gene was sequenced and determined (GenBank accession No. AB698450.1). Wu et al. (2009) also reviewed an AF degradation enzyme from *P. ostreatus* in the earlier time, and an enzyme named aflatoxin-detoxifizyme (ADTZ) from *Armillariella tabescens* (E-20).

Zhao et al. (2011) prepared and purified an extracellular enzyme, designated as myxobacteria aflatoxin degradation enzyme (MADE), from bacterium *M. fulvus* ANSM068 with a final specific activity of 569.44×10^3 U/mg. The pure enzyme (100 U/mL) demonstrated high degradation ability against AFG_1 (96.96%) and AFM_1 (95.80%) after 48 h of incubation. Enzyme MADE demonstrated high activity in a broad range of pH values between 5.0 and 7.0, and temperatures between 30 and 45°C.

Recombinant laccase produced by *A. niger* D15-Lcc2#3 (118 U/L) decreased AFB_1 by 55% in 72 h (Alberts et al., 2009). Aflatoxin-detoxifizyme ADTZ from *A. tabescens* was confirmed to be an oxidase and renamed aflatoxin-oxidase (AFO). Wen et al. (2011) cloned the cDNA of AFO, and expressed this gene as a fusion protein in *Pichia pastoris* by using pPIC9-afo as vector. The recombinant AF oxidase converted AFB_1 with the K_m value of $3.93 \pm 0.20 \times 10^{-6}$ mol/L under its optimal conditions of pH 6.0 and 30°C.

3. Biological degradation of zearalenone

3.1. Fungi

Some fungi that exhibit degradation ability against ZEA have been reviewed by Zinedine et al. (2007). Indeed, *Thamnidium elegans* (NRRL 1613) and *Mucor bainieri* (NRRL 2988) could transform ZEA into a non-estrogenic substance ZEA-4-O-β-glucoside. Zearalenone was converted to 8′-hydroxy-zearalenone and 2, 4-dimethoxyzearalenone by *Streptomyces rimosus* (NRRL 2234) and *Cunninghamella bainieri* (ATCC 9244B), respectively. *Gliocladium roseum* (synonym: *Clonostachys rosea*) could cleave the lactone ring of ZEA, and result in subsequent spontaneous decarboxylatioin, rendering the reaction irreversible. Utermark and Karlovsky (2007) also reported that *G. roseum* produced a zearalenone-specific lactonase which protected *G. roseum* from the inhibitory and toxic effects of ZEA. The lactonase could catalyze the hydrolysis of ZEA, followed by a spontaneous decarboxylation. *Trichosporon mycotoxinivorans* had a very high capability to degrade ZEA. Furthermore, the metabolite of ZEA by *T. mycotoxinivorans* has been investigated by Vekiru et al. (2010). The authors reported that the novel ZEA metabolite, named ZOM-1, was characterized by an opening of the macrocyclic ring of ZEA at the ketone group at C6′, and identified as (5S)-5-({2,4-dihydroxy-6-[(1E)-5-hydroxypent-1-en-1-yl]benzoyl}oxy) hexanoic acid. In addition, the ZOM-1 metabolite was not estrogenic *in vivo* and did not interact *in vitro* with the estrogen receptor protein, showing the loss of ZOM-1 estrogenicity. Zearalenone was found to be completely degraded by several *Rhizopus* isolates including *R. stolonifer*, *R. oryzae* and *Rhizopus microsporus* strains. El-Sharkaway et al. (1991) demonstrated that *R. arrhizus* (IFO-6155) could catalyze sulfation of ZEA at the C-4 hydroxyl group, forming a new metabolite determined as ZEA-4-O-sulfate conjugate. As well, *A. niger* was able to detoxify ZEA by sulfonation, leading to a less toxic compound (Jard et al., 2010).

3.2. Bacteria

A few studies on the bio-transformation of ZEA by bacteria have been reported, and the strains in these studies include the bacterial gut flora of pigs (Kollarczik et al., 1994), mixed culture (*Alcaligenes*, *Bacillus*, *Achromobacter*, *Flavobacterium*, and *Pseudomonas*)

(Megharaj et al., 1997), *Acinetobacter* sp (Yu et al., 2011a). and so on. Recently, Cserháti et al. (2013) have reported that three *Rhodococcus* species *R. erythropolis*, *Rhodococcus ruber* and *Rhodococcus pyridinivorans* had >50% ZEA degrading capacity, thereinto, *R. pyridinivorans* strains were the most effective degraders with 70% efficiency. *Pseudomonas* bacteria are also capable of ZEA biodegradation. Tan et al. (2014) isolated two ZEA degrading bacteria from gyttja soil and moldy soil, named as *Pseudomonas alcaliphila* TH-C1 and *Pseudomonas*. *plecoglossicida* TH-L1, and their degradation rate for ZEA (2 μg/mL) was about 68% and 57%, respectively, when incubated for 72 h. Altalhi (2007) described a *Pseudomonas* strain, *Pseudomonas putida* ZEA-1 isolated from rhizosphere of corn plant, is able to utilize ZEA as energy source and transform ZEA along with its derivatives, including α- and β-zearalenol, without generating harmful metabolites. Later, Altalhi and El-Deeb (2009) localized and cloned the fragment containing genes encoding for ZEA detoxification in the plasmid of *P. putida* ZEA-1, and the cloned genes were actively expressed in *E. coli*. The results showed that ZEA degradation by recombinant *E. coli* was relatively rapid and effective, leaving no detectable ZEA after 24 h. There were more than one target proteins induced through growth of recombinant *E. coli*, however, the authors were unable to separate these genes, indicating that the genes are organized in a complex structure and probably the degradative genes are clustered in one or more large operons in bacteria. The efficient abilities of *B. licheniformis* CK1 (Yi et al., 2011) and *B. subtilis* (Cho et al., 2010) to degrade ZEA in the culture media were also reported. Our research team screened a strain of bacteria *B. subtilis* ANSB01G from normal broiler intestinal chyme, which could reduce ZEA by 88.65% (Lei et al., 2014). Under simulated intestinal tract conditions, the *B. subtilis* ANSB01G degraded 84.58%, 66.34% and 83.04% of ZEA in naturally contaminated corn, distiller's dried grains with solubles (DDGS) and swine complete feed, respectively. Moreover, the addition of ANSB01G to diet naturally contaminated with ZEA obviously ameliorated adverse symptoms induced by ZEA in prepubertal female gilts (Zhao et al., 2015).

3.3. Enzyme

Takahashi-Ando et al. (2002) purified a novel lactonohydrolase in fungus *C. rosea* that is responsible for the detoxification of ZEA, and then cloned the encoding gene, designated as *zhd101.* Maximal activity of recombinant ZHD101 protein expressed in *E. coli* toward ZEA was observed at pH 10.5 with an extremely low molar activity ($k_{cat} = 0.51$/s at 30°C) (Takahashi-Ando et al., 2004). Yu et al. (2011b) isolated enzymes from bacterium *Acinetobacter* sp. SM04 extracellular extracts of liquid cultures, and obtained an active fraction capable of efficiently degrading ZEA. The active fraction could degrade ZEA into smaller estrogenic products, and two intermediate products, ZEN-1 and ZEN-2, were found, which indicated that the benzene ring of zearalenone may be cleaved and oxidized into the products containing carboxyl groups. Further, enzymes in the active fraction were analyzed, and three proteins were found. They were identified as peroxiredoxin, a possible cytochrome and aputative fimbrial protein precursor.

4. Biological degradation of deoxynivalenol

4.1. Fungi

It was reported that the growing *Fusarium nivale* acetylated DON to afford a small amount of 3-acetyldeoxynivalenol (Yoshizawa and Morooka, 1975). The fungus *Aspergillus tubingensis NJA-1*, isolated from soil, demonstrated an ability to degrade DON. And the molecular weight of the bioconversion metabolite was 18.1 D (H_2O) larger than that of DON, showing that DON could be hydrolyzed by *NJA-1* (He et al., 2008).

4.2. Bacteria

To date, several microorganisms from various sources such as soils, animal guts, and plants have been reported to have the ability to degrade DON. Zhou et al. (2008), He et al. (2010), Awad et al. (2010) and Karlovsky (2011) have reviewed the studies on DON degradation. Shima et al. (1997) inferred that 3-OH group in DON is likely to be involved in exerting its immunosuppressive toxicity. *Agrobacterium–Rhizobium* strain E3-39 was obtained from soil samples by an enrichment culture procedure (Shima et al., 1997). The strain E3-39 could oxidize the 3-OH group of DON to generate 3-keto-4-deoxynivalenol (3-keto-DON), which exhibited a remarkably decreased (to less than one tenth) immunosuppressive toxicity relative to DON. Among 1,285 microbial cultures obtained from farmland soils, cereal grains, insects and other sources, Völkl et al. (2004) screened one mixed culture from spontaneously infected minimal medium with protein and glucose (MMGP), able to transform DON into 3-keto-DON. The strain could also transform trichothecenes 15-acetyl-DON, 3-acetyl-DON and fusarenon-X. However, the microorganisms responsible for the biotransformation have not been identified. The bacterium *Nocardioides* WSN05-2, isolated from soil samples collected in wheat fields, degraded DON to produce a novel intermediate, 3-*epi*-DON (Ikunaga et al., 2011). 3-*epi*-DON is an epimer of DON, which is different from DON in the stereochemistry at the 3-OH group. Recently, He et al. (2015) screened a bacterium *Devosia mutans* 17-2-E-8 from an agricultural soil. The bacterium was capable of transforming DON to 3-*epi*-DON (major product) and 3-keto-DON (minor product). And the metabolite 3-*epi*-DON was proved to be less toxic than DON through *in vitro* and *in vivo* studies. A total of thirteen aerobic DON-degrading bacteria were isolated from a variety of environmental samples, including field soils and wheat leaves (Sato et al., 2012). Of these thirteen strains, nine belonged to the Gram-positive genus *Nocardioides* and other four to the Gram-negative genus *Devosia*, indicating that aerobic DON-degrading bacteria were distributed within at least two phylogenetically restricted genera.

Microorganisms in rumen fluid from different ruminants could transform DON. The C-12, 13-epoxy group is essential for the toxicity of DON. Yoshizawa et al. (1983) were the first to characterize the deepoxidated metabolite of DON, namely DOM-1, in rat urine and feces. The rumen fluid from a cow transformed all DON (up to 10 ppm) to DOM-1 within a 24-h period (King et al., 1984). The deepoxidation of DON by rumen fluid was also described by Côté et al. (1986) and Swanson et al. (1987). So far, *Eubacterium* strain BBSH 797 is the most intensively studied bacterial isolate able to transform DON. The strain was isolated from cow rumen fluid (He et al., 1992) and its capability of transforming DON into DOM-1 was proven *in vitro* and *in vivo* (Schatzmayr et al., 2006; Zhou et al., 2008). Fuchs et al. (2002) found that *Eubacterium* BBSH 797 could transform the epoxide group of trichothecenes into a diene. A BBSH 797-based commercial mycotoxin-deactivating feed additive product is available on the market. Awad et al. (2004, 2006) demonstrated that the *Eubacterium* sp. DSM 11798 could counteract the adverse effect of DON on poultry.

In the past three decades, transformation of DON by microorganisms from animal intestines has also been studied. Lun et al. (1988) observed a decrease in DON, when it is incubated with the fluids obtained from the main parts of hen gastrointestinal tract. Microbiota from chicken large intestines (He et al., 1992) and pure cultures of microbial isolates (LS100 and SS3) from chicken intestine (Young et al., 2007) showed the capacity for degrading DON by deepoxidation. Yu et al. (2010) utilized conventional

microbiological selection strategies guided by PCR-DGGE (denaturing gradient gel electrophoresis) bacterial profiles to isolate DON-transforming bacteria. And 16S rRNA gene sequence analysis indicated that the ten isolates obtained belong to four different bacterial groups, *Clostridiales*, *Anaerofilum*, *Collinsella*, and *Bacillus*. Moreover, *Bacillus* sp. LS100 could detoxify DON in contaminated feed before feeding pigs and thus completely eliminate the adverse effects of DON on pigs (Li et al., 2011). Studies have also shown that DON can be transformed to DOM-1 by intestinal microorganisms of other animal species including rat (Worrell et al., 1989) and pig (Kollarczik et al., 1994). In addition, Guan et al. (2009) screened one microbial community from catfish (*Ameiurus nebulosus*) digesta, namely microbial culture C133, completely transforming DON to de-epoxy-DON after 96 h incubation.

4.3. Enzyme

3-O-acetylation of the trichothecene ring in DON leads to its inactivation. Gene *Tri101* encoding trichothecene-3-O-acetyltransferase from *F. graminearum* was characterized (Kimura et al., 1998). Khatibi et al. (2011) cloned trichothecene 3-O-acetyltransferases genes from seven *Fusarium* species and compared the properties of them to identify an optimal source of the enzyme for biotechnological applications. A UDP-glucosyltransferase from *Arabidopsis thaliana* catalyzed transfer of glucose from UDP-glucose to the hydroxyl group at carbon 3 of DON (Poppenberger et al., 2003). However, whether acetylation of C3-OH or conjugation by glycosylation can be considered as detoxification is controversial, because acetylated and conjugated mycotoxins may be hydrolyzed and regenerated the toxins in the digestive system of animals and humans.

5. Perspective

Microbial detoxification may become a promising choice, since it can be a specific, effective, irreversible and environmental friendly strategy of detoxification that leaves no toxic residues. Despite the many publications on biological transformation of mycotoxins by microorganisms, their application in practice in detoxification of food and/or feed has been limited. Practical applications of fungi may be limited by factors, such as complicated procedures needed for obtaining the active extracts, long incubation time required for the detoxification, and incomplete detoxification process. The high degradation rate and wide reaction conditions for degradation by bacteria imply a potential and promising application for mycotoxin degradation. Innovative techniques and strategies, such as enrichments, highly selective media, PCR-DGGE bacterial profiles and effective molecular techniques, may increase the opportunities to select target microorganisms from a complex microflora. It is also of great interest to develop studies focusing on probiotic bacteria, which can be directly applied in the feedstuffs and feeds. In addition, the use of active enzyme(s) seems to be a promising opportunity for mycotoxins degradation. Many enzymes with certain function, such as phytase, have been purified from fermentation broth, and successfully applied in food and feed industries. In this respect, enzyme products for the effective detoxification of mycotoxins can be developed through preparation and purification of enzyme, identification of the genes encoding the enzyme, and overexpression of the recombinant enzyme. Meanwhile, the studies on mechanisms of biodegradation, structure of degradation products, and safety of the microorganisms and degradation products towards animals are still warranted to support the application of microorganisms in food and feed industry.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (31301981), Special Fund for Agro-scientific Research in the Public Interest (201403047), Beijing Municipal Natural Science Foundation (Grant No. 6132021), and the National Key Technology Research and Development Program of the Ministry of Science and Technology of China (Grant No. 2013BAD10B02, 2012BAD39B00).

References

Alberts JF, Gelderblom WCA, Botha A, van Zyl WH. Degradation of aflatoxin B_1 by fungal laccase enzymes. Int J Food Microbiol 2009;135(1):47–52.
Altalhi AD. Plasmid-mediated detoxification of mycotoxin zearalenone in *Pseudomonas* sp. ZEA-1. Am J Biochem Biotechnol 2007;3(3):150–8.
Altalhi AD, El-Deeb B. Localization of zearalenone detoxification gene(s) in pZEA-1 plasmid of *Pseudomonas putida* ZEA-1 and expressed in *Escherichia coli*. J Hazard Mater 2009;161(2):1166–72.
Awad WA, Böhm J, Razzazi-Fazeli E, Ghareeb K, Zentek J. Effect of addition of a probiotic microorganism to broiler diets contaminated with deoxynivalenol on performance and histological alterations of intestinal villi of broiler chickens. Poult Sci 2006;85(6):974–9.
Awad WA, Böhm J, Razzazi-Fazeli E, Hulan HW, Zentek J. Effects of deoxynivalenol on general performance and electrophysiological properties of intestinal mucosa of broiler chickens. Poult Sci 2004;83(12):1964–72.
Awad WA, Ghareeb K, Böhm J, Zentek J. Decontamination and detoxification strategies for the fusarium mycotoxin deoxynivalenol in animal feed and the effectiveness of microbial biodegradation. Food Addit Contam 2010;27(4):510–20.
Bata Á, Lásztity R. Detoxification of mycotoxin-contaminated food and feed by microorganisms. Trends Food Sci Technol 1999;10(6):223–8.
Borutova R, Aragon YA, Nährer K, Berthiller F. Co-occurrence and statistical correlations between mycotoxins in feedstuffs collected in the Asia-Oceania in 2010. Animal Feed Sci Technol 2012;178(3–4):190–7.
Bryden WL. Mycotoxin contamination of the feed supply chain: implications for animal productivity and feed security. Animal Feed Sci Technol 2012;173(1–2):134–58.
Cho KJ, Kang JS, Cho WT, Lee CH, Ha JK, Song KB. *In vitro* degradation of zearalenone by *Bacillus subtilis*. Biotechnol Lett 2010;32(12):1921–4.
Ciegler A, Lillehoj EB, Peterson RE, Hall HH. Microbial detoxification of aflatoxin. Appl Microbiol 1966;14(6):934.
Cole RJ, Blankens BR, Kirksey JW. Conversion of aflatoxin B_1 to isomeric hydroxy compounds by *Rhizopus* spp. J Agric Food Chem 1972;20(6):1100.
Cole RJ, Kirksey JW. Aflatoxin G_1 metabolism by *Rhizopus* species. J Agric Food Chem 1971;19(2):222.
Côté LM, Nicoletti J, Swanson SP, Buck WB. Production of deepoxydeoxynivalenol (DOM-1), a metabolite of deoxynivalenol, by *in vitro* rumen incubation. J Agric Food Chem 1986;34(3):458–60.
Council for Agricultural Science and Technology (CAST). Mycotoxins: risks in plant, animal, and human systems. Ames, IA: Council for Agricultural Science and Technology; 2002.
Cserháti M, Kriszt B, Krifaton C, Szoboszlay S, Hahn J, Toth S, et al. Mycotoxin-degradation profile of *Rhodococcus* strains. Int J Food Microbiol 2013;166(1):176–85.
Detroy RW, Hesselti CW. Transformation of aflatoxin B_1 by steroid-hydroxylating fungi. Can J Microbiol 1969;15(6):495.
Doyle MP, Marth EH. Aflatoxin is degraded by heated and unheated mycelia, filtrates of homogenized mycelia and filtrates of broth cultures of *Aspergillus parasiticus*. Mycopathologia 1978;64(1):59–62.
El-Sharkaway SH, Selim MI, Afifi MS, Halaweish FT. Microbial transformation of zearalenone to a zearalenone sulfate. Appl Environ Microbiol 1991;57(2):549–52.
Fan Y, Zhao L, Ji C, Li X, Jia R, Xi L, et al. Protective Effects of *Bacillus subtilis* ANSB060 on serum biochemistry, histopathological changes and antioxidant enzyme activities of broilers fed moldy peanut meal naturally contaminated with aflatoxins. Toxins 2015;7(8):3330–43.
Fan Y, Zhao L, Ma Q, Li X, Shi H, Zhou T, et al. Effects of *Bacillus subtilis* ANSB060 on growth performance, meat quality and aflatoxin residues in broilers fed moldy peanut meal naturally contaminated with aflatoxins. Food Chem Toxicol 2013;59:748–53.
Farzaneh M, Shi Z, Ghassempour A, Sedaghat N, Ahmadzadeh M, Mirabolfathy M, et al. Aflatoxin B_1 degradation by *Bacillus subtilis* UTBSP1 isolated from pistachio nuts of Iran. Food Control 2012;23(1):100–6.
Fuchs E, Binder EM, Heidler D, Krska R. Structural characterization of metabolites after the microbial degradation of type A trichothecenes by the bacterial strain BBSH 797. Food Addit Contam 2002;19(4):379–86.
Gao X, Ma Q, Zhao L, Lei Y, Shan Y, Ji C. Isolation of *Bacillus subtilis*: screening for aflatoxins B_1, M_1, and G_1 detoxification. Eur Food Res Technol 2011;232(6):957–62.
Gholami-Ahangaran M, Rangsaz N, Azizi S. Evaluation of turmeric (*Curcuma longa*) effect on biochemical and pathological parameters of liver and kidney in chicken aflatoxicosis. Pharm Biol 2016;54(5):780–7.

Guan S, Yin Y, Zhou T, Xie M, Ruan Z, Young JC. Microbial strategies to control aflatoxins in food and feed. World Mycotoxin J 2011;4:413–24.

Guan S, He J, Young JC, Zhu H, Li X, Ji C, et al. Transformation of trichothecene mycotoxins by microorganisms from fish digesta. Aquaculture 2009;290(3):290–5.

Guan S, Ji C, Zhou T, Li J, Ma Q, Niu T. Aflatoxin B_1 degradation by *Stenotrophomonas maltophilia* and other microbes selected using coumarin medium. Int J Mol Sci 2008;9(8):1489–503.

Guan S, Zhao L, Ma Q, Zhou T, Wang N, Hu X, et al. *In vitro* efficacy of *Myxococcus fulvus* ANSM068 to biotransform aflatoxin B_1. Int J Mol Sci 2010;11(10):4063–79.

He C, Fan Y, Liu G, Zhang H. Isolation and identification of a strain of *Aspergillus tubingensis* with deoxynivalenol biotransformation capability. Int J Mol Sci 2008;9(12):2366–75.

He J, Bondy GS, Zhou T, Caldwell D, Boland GJ, Scott PM. Toxicology of 3-*epi*-deoxynivalenol, a deoxynivalenol-transformation product by *Devosia mutans* 17-2-E-8. Food Chem Toxicol 2015;84:250–9.

He J, Zhou T, Young JC, Boland GJ, Scott PM. Chemical and biological transformations for detoxification of trichothecene mycotoxins in human and animal food chains: a review. Trends Food Sci Technol 2010;21(2):67–76.

He P, Young LG, Forsberg C. Microbial transformation of deoxynivalenol (vomitoxin). Appl Environ Microbiol 1992;58(12):3857–63.

Huynh VL, Gerdes RG, Lloyd AB. Synthesis and degradation of aflatoxins by *Aspergillus parasiticus*. II. Comparative toxicity and mutagenicity of aflatoxin B_1 and its autolytic breakdown products. Aust J Biol Sci 1984;37(3):123–9.

Ikunaga Y, Koitabashi M, Ito M, Karlovsky P, Tsushima S, Sato I, et al. *Nocardioides* sp. strain WSN05-2, isolated from a wheat field, degrades deoxynivalenol, producing the novel intermediate 3-*epi*-deoxynivalenol. Appl Microbiol Biotechnol 2011;89(2):419–27.

Jard G, Liboz T, Mathieu F, Guyonvarc'H A, Andre F, Delaforge M, et al. Transformation of zearalenone to zearalenone-sulfate by *Aspergillus* spp. World Mycotoxin J 2010;3(2):183–91.

Karlovsky P. Biological detoxification of the mycotoxin deoxynivalenol and its use in genetically engineered crops and feed additives. Appl Microbiol Biotechnol 2011;91(3):491–504.

Khatibi PA, Newmister SA, Rayment I, Susan PM, Nancy JA, David GSI. Bioprospecting for trichothecene 3-O-acetyltransferases in the fungal genus *Fusarium* yields functional enzymes with different abilities to modify the mycotoxin deoxynivalenol. Appl Environ Microbiol 2011;77(4):1162–70.

Kimura M, Matsumoto G, Shingu Y, Yoneyama K, Yamaguchi I. The mystery of the trichothecene 3-O-acetyltransferase gene: analysis of the region around *Tri101* and characterization of its homologue from *Fusarium sporotrichioides*. FEBS Lett 1998;435(2–3):163–8.

King RR, McQueen RE, Levesque D, Greenhalgh R. Transformation of deoxynivalenol (vomitoxin) by rumen microorganisms. J Agric Food Chem 1984;32(5):1181–3.

Kollarczik B, Gareis M, Hanelt M. *In vitro* transformation of the fusarium mycotoxins deoxynivalenol and zearalenone by the normal gut microflora of pigs. Nat Toxins 1994;2(3):105–10.

Kong Q, Zhai C, Guan B, Li C, Shan S, Yu J. Mathematic modeling for optimum conditions on aflatoxin B_1 degradation by the aerobic bacterium *Rhodococcus erythropolis*. Toxins 2012;4(11):1181–95.

Kusumaningtyas E, Widiastuti R, Maryam R. Reduction of aflatoxin B_1 in chicken feed by using *Saccharomyces cerevisiae*, *Rhizopus oligosporus* and their combination. Mycopathologia 2006;162(4):307–11.

Lapalikar GV, Taylor MC, Warden AC, Scott C, Russell RJ, Oakeshott JG. $F_{420}H_2$-dependent degradation of aflatoxin and other furanocoumarins is widespread throughout the *Actinomycetales*. Plos One 2012;7:e301142.

Lei YP, Zhao LH, Ma QG, Zhang JY, Zhou T, Gao CQ, et al. Degradation of zearalenone in swine feed and feed ingredients by *Bacillus subtilis* ANSB01G. World Mycotoxin J 2014;7(2):143–51.

Li X, Zhao L, Fan Y, Jia Y, Sun L, Ma S, et al. Occurrence of mycotoxins in feed ingredients and complete feeds obtained from the Beijing region of China. J Animal Sci Biotechnol 2014;5(1):37–44.

Li XZ, Zhu C, de Lange CFM, Zhou T, He J, Yu H, et al. Efficacy of detoxification of deoxynivalenol-contaminated corn by *Bacillus* sp. LS100 in reducing the adverse effects of the mycotoxin on swine growth performance. Food Addit Contam 2011;28(7):894–901.

Lun AK, Moran JET, Young LG, McMillan EG. Disappearance of deoxynivalenol from digesta progressing along the chicken's gastrointestinal tract after intubation with feed containing contaminated corn. Bull Environ Contam Toxicol 1988;40(3):317–24.

Ma QG, Gao X, Zhou T, Zhao LH, Fan Y, Li XY, et al. Protective effect of *Bacillus subtilis* ANSB060 on egg quality, biochemical and histopathological changes in layers exposed to aflatoxin B_1. Poult Sci 2012;91(11):2852–7.

Mann R, Rehm HJ. Degradation products from aflatoxin B_1 by *Corynebacterium rubrum, Aspergillus niger, Trichoderma viride* and *Mucor ambiguus*. Eur J Appl Microbiol 1976;2:297–306.

Maresca M. From the gut to the brain: journey and pathophysiological effects of the food-associated trichothecene mycotoxin deoxynivalenol. Toxins 2013;5(4):784–820.

Megharaj M, Garthwaite I, Thiele JH. Total biodegradation of the oestrogenic mycotoxin zearalenone by a bacterial culture. Lett Appl Microbiol 1997;24(5):329–33.

Miazzo R, Dalcero A, Rosa CA, De Queiroz Carvalho EC, Magnoli C, Chiacchiera SM, et al. Efficacy of synthetic zeolite to reduce the toxicity of aflatoxin in broiler chicks. Poult Sci 2000;79(1):1–6.

Mishra HN, Das C. A review on biological control and metabolism of aflatoxin. Crit Rev Food Sci Nutr 2003;43(3):245.

Mishra S, Ansari KM, Dwivedi PD, et al. Occurrence of deoxynivalenol in cereals and exposure risk assessment in Indian population. Food Control 2013;30(2):549–55.

Mohamed EZ. Impact of mycotoxins on humans and animals. J Saudi Chem Soc 2011;15(2):129–44.

Nakazato M, Saito K, Kikuchi Y, Ibe A, Fujinuma K, Nishijima M, et al. Conversion of aflatoxin B_1 to aflatoxicols by various fungi isolated from aflatoxicols contaminating corn. Food Hyg Saf Sci 1985;26:33–8.

Oueslati S, Romero-Gonzalez R, Lasram S, Frenich AG, Vidal JLM. Multi-mycotoxin determination in cereals and derived products marketed in Tunisia using ultra-high performance liquid chromatography coupled to triple quadrupole mass spectrometry. Food Chem Toxicol 2012;50(7):2376–81.

Petchkongkaew A, Taillandier P, Gasaluck P, Lebrihi A. Isolation of *Bacillus* spp. from Thai fermented soybean (Thua-nao): screening for aflatoxin B_1 and ochratoxin A detoxification. J Appl Microbiol 2008;104(5):1495–502.

Pitt JI. Toxigenic fungi and mycotoxins. Br Med Bull 2000;56(1):184–92.

Poppenberger B, Berthiller F, Lucyshyn D, Sieberer T, Rainer S, Rudolf K, et al. Detoxification of the fusarium mycotoxin deoxynivalenol by a UDP-glucosyltransferase from *Arabidopsis thaliana*. J Biol Chem 2003;278(48):47905–14.

Sangare L, Zhao Y, Folly YME, Chang J, Li J, Selvaraj JN, et al. Aflatoxin B_1 degradation by a *Pseudomonas* strain. Toxins 2014;6(10):3028–40.

Sato I, Ito M, Ishizaka M, Ikunaga Y, Sato Y, Yoshida S, et al. Thirteen novel deoxynivalenol-degrading bacteria are classified within two genera with distinct degradation mechanisms. FEMS Microbiol Lett 2012;327(2):110–7.

Schatzmayr G, Zehner F, Taeubel M, Schatzmayr D, Klimitsch A, Loibner AP, et al. Microbiologicals for deactivating mycotoxins. Mol Nutr Food Res 2006;50(6):543–51.

Schoevers EJ, Santos RR, Colenbrander B, et al. Transgenerational toxicity of zearalenone in pigs. Reprod Toxicol 2012;34(1):110–9.

Shantha T. Fungal degradation of aflatoxin B_1. Nat Toxins 1999;7(5):175–8.

Shima J, Takase S, Takahashi Y, Iwai Y, Fujimoto H, Yamazaki M, et al. Novel detoxification of the trichothecene mycotoxin deoxynivalenol by a soil bacterium isolated by enrichment culture. Appl Environ Microbiol 1997;63(10):3825–30.

Stoev SD. Foodborne mycotoxicoses, risk assessment and underestimated hazard of masked mycotoxins and joint mycotoxin effects or interaction. Environ Toxicol Pharmacol 2015;39(2):794–809.

Stoev SD. Food safety and increasing hazard of mycotoxin occurrence in foods and feeds. Crit Rev Food Sci Nutr 2013;53(9):887–901.

Streit E, Naehrer K, Rodrigues I, Schatzmayr G. Mycotoxin occurrence in feed and feed raw materials worldwide: long-term analysis with special focus on Europe and Asia. J Sci Food Agric 2013;93(12):2892–9.

Swanson SP, Nicoletti J, Rood HJ, Buck WB, Marie Cote L, Yoshizawa T. Metabolism of three trichothecene mycotoxins, T-2 toxin, diacetoxyscirpenol and deoxynivalenol, by bovine rumen microorganisms. J Chromatogr 1987;414(2):335–42.

Takahashi-Ando N, Kimura M, Kakeya H, Osada H, Yamaguchi I. A novel lactonohydrolase responsible for the detoxification of zearalenone: enzyme purification and gene cloning. Biochem J 2002;365(Pt 1):1–6.

Takahashi-Ando N, Ohsato S, Shibata T, Hamamoto H, Isamu Y, Makoto K. Metabolism of zearalenone by genetically modified organisms expressing the detoxification gene from *Clonostachys rosea*. Appl Environ Microbiol 2004;70(6):3239–45.

Tan H, Zhong Z, Peng G, Deng J, Hu Y, He J, et al. Zearalenone degradation by two *Pseudomonas* strains from soil. Mycotoxin Res 2014;30(4):191–6.

Taylor MC, Jackson CJ, Tattersall DB, French N, Peat TS, Newman J, et al. Identification and characterization of two families of $F_{420}H_2$-dependent reductases from *Mycobacteria* that catalyse aflatoxin degradation. Mol Microbiol 2010;78(3):561–75.

Taylor WJ, Draughon FA. Nannocystis exedens: a potential biocompetitive agent against *Aspergillus flavus* and *Aspergillus parasiticus*. J Food Prot 2001;64(7):1030–4.

Utermark J, Karlovsky P. Role of zearalenone lactonase in protection of *Gliocladium roseum* from fungitoxic effects of the mycotoxin zearalenone. Appl Environ Microbiol 2007;73(2):637–42.

Vekiru E, Hametner C, Mitterbauer R, Rechthaler J, Gerhard A, Gerd S, et al. Cleavage of zearalenone by *Trichosporon mycotoxinivorans* to a novel nonestrogenic metabolite. Appl Environ Microbiol 2010;76(7):2353–9.

Völkl A, Vogler B, Schollenberger M, Karlovsky P. Microbial detoxification of mycotoxin deoxynivalenol. J Basic Microbiol 2004;44(2):147–56.

Wang J, Ogata M, Hirai H, Kawagishi H. Detoxification of aflatoxin B_1 by manganese peroxidase from the white-rot fungus *Phanerochaete sordida* YK-624. FEMS Microbiol Lett 2011;314(2):164–9.

Wen S, Guan M, Zhou T, Gao H, Xie C, Liu D, et al. Cloning, expression, purification and characterization of an aflatoxin-converting enzyme from *Armillaria tabescens*. Weishengwu Xuebao 2011;51(9):1212–21.

Williams JG, Deschl U, Williams GM. DNA damage in fetal liver cells of Turkey and chicken eggs dosed with aflatoxin B_1. Archives Toxicol 2011;85(9):1167–72.

Wogan GN, Pong RS. Aflatoxins. Ann N Y Acad Sci 1970;174(2):623–35.

Worrell NR, Mallett AK, Cook WM, Baldwin N, Shepherd MJ. The role of gut micro-organisms in the metabolism of deoxynivalenol administered to rats. Xenobiotica 1989;19(1):25–32.

Wu L, Liao P, He LQ, et al. Growth performance, serum biochemical profile, jejunal morphology, and the expression of nutrients transporter genes in deoxynivalenol (DON)-challenged growing pigs. BMC Vet Res 2015a;11:144–54.

Wu Q, Jezkova A, Yuan Z, Pavlikova L, Dohnal V, Kuca K. Biological degradation of aflatoxins. Drug Metab Rev 2009;41(1):1–7.
Wu Li, Liao Peng, He Liuqin, Feng Zemeng, Ren Wenkai, Yin Jie, et al. Dietary L-Arginine supplementation protects weanling pigs from deoxynivalenol-induced toxicity. Toxins 2015b;7:1341–54.
Wu L, Wang W, Yao K, et al. Effects of dietary arginine and glutamine on alleviating the impairment induced by deoxynivalenol stress and immune relevant cytokines in growing pigs. Plos One 2013;8:e69502.
Wu Miaomiao, Xiao Hao, Ren Wenkai, Yin Jie, Hu Jiayu, Duan Jielin, et al. An NMR-based metabolomic approach to investigate the effects of supplementation with glutamic acid in piglets challenged with deoxynivalenol. Plos One 2014;9:0113687.
Yehia RS. Aflatoxin detoxification by manganese peroxidase purified from *Pleurotus ostreatus*. Braz J Microbiol 2014;45(1):127–33.
Yi P, Pai C, Liu J. Isolation and characterization of a *Bacillus licheniformis* strain capable of degrading zearalenone. World J Microbiol Biotechnol 2011;27(5):1035–43.
Yoshizawa T, Morooka N. Biological modification of trichothecene mycotoxins: acetylation and deacetylation of deoxynivalenols by *Fusarium* spp. Appl Microbiol 1975;29(1):54–8.
Yoshizawa T, Takeda H, Ohi T. Structure of a novel metabolite from deoxynivalenol, a trichothecene mycotoxin, in animals. Agric Biol Chem 1983;47(9):2133–5.
Young JC, Zhou T, Yu H, Zhu H, Gong J. Degradation of trichothecene mycotoxins by chicken intestinal microbes. Food Chem Toxicol 2007;45(1):136–43.
Yu H, Zhou T, Gong J, Young C, Su X, Li X, et al. Isolation of deoxynivalenol-transforming bacteria from the chicken intestines using the approach of PCR-DGGE guided microbial selection. BMC Microbiol 2010;10(1):182.
Yu Y, Qiu L, Wu H, Tang Y, Yu Y, Li X, et al. Degradation of zearalenone by the extracellular extracts of *Acinetobacter* sp. SM04 liquid cultures. Biodegradation 2011a;22(3):613–22.
Yu Y, Qiu L, Wu H, Tang Y, Lai F, Yu Y. Oxidation of zearalenone by extracellular enzymes from *Acinetobacter* sp. SM04 into smaller estrogenic products. World J Microbiol Biotechnol 2011b;27(11):2675–81.
Zeinvand-Lorestani H, Sabzevari O, Setayesh N, Amini M, Nili-Ahmadabadi A, Faramarzi MA. Comparative study of *in vitro* prooxidative properties and genotoxicity induced by aflatoxin B_1 and its laccase-mediated detoxification products. Chemosphere 2015;135:1–6.
Zhang W, Xue B, Li M, Mu Y, Chen Z, Li J, et al. Screening a strain of *Aspergillus niger* and optimization of fermentation conditions for degradation of aflatoxin B_1. Toxins 2014;6(11):3157–72.
Zhao L, Lei Y, Bao Y, Jia R, Ma Q, Zhang J, et al. Ameliorative effects of *Bacillus subtilis* ANSB01G on zearalenone toxicosis in pre-pubertal female gilts. Food Addit Contam 2015;32(4):617–25.
Zhao LH, Guan S, Gao X, Ma QG, Lei YP, Bai XM, et al. Preparation, purification and characteristics of an aflatoxin degradation enzyme from *Myxococcus fulvus* ANSM068. J Appl Microbiol 2011;110(1):147–55.
Zhou T, He J, Gong J. Microbial transformation of trichothecene mycotoxins. World Mycotoxin J 2008;1(1):23–30.
Zinedine A, Soriano JM, Moltó JC, Mañes J. Review on the toxicity, occurrence, metabolism, detoxification, regulations and intake of zearalenone: an oestrogenic mycotoxin. Food Chem Toxicol 2007;45(1):1–18.