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Review Article

Current review of biodegradation and detoxification strategies for zearalenone contaminated food and feed

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Abstract: Mycotoxins are toxic metabolites produced by fungi that may cause serious health problems in humans and animals. Zearalenone is an estrogenic mycotoxin produced by *Fusarium* species that leads to huge economic losses in the food industry and livestock husbandry. Contamination of food and feed with zearalenone has reproductive problems, carcinogenicity, immunotoxicity, and other cytotoxic effects. At present, microorganisms and enzymes derived from microbial strains have been widely used for the degradation of zearalenone in food and feed. Researchers have developed biodegradation of zearalenone by the use of microbial and their enzyme derivatives, which offers harmless products and is environmentally friendly. Development of recombinant enzymes improves enzymatic detoxification of zearalenone to a non-toxic product without damaging the nutritional content. This review summarizes biodegradation and detoxification strategies of zearalenone using microorganisms and enzyme derivatives to nontoxic products.

1. INTRODUCTION

Mycotoxins are naturally occurring toxic secondary metabolites of some microscopic filamentous fungi (Liu *et al.*, 2022). Mycotoxins produced mainly by some fungal species belonging to *Alternaria*, *Aspergillus*, *Fusarium,* and *Penicillium* genera pose health threats to humans and animals (Greeff-Laubscher *et al.*, 2020). Mycotoxins contamination of foods and feeds is a current global issue and causes huge economic losses to animal husbandry (Navale & Vamkudoth, 2022). More than 400 different types of mycotoxins have been identified so far, with different levels of toxicity (Arroyo-Manzanares *et al.*, 2021). Among all mycotoxins, Aflatoxins B1, Zearalenone, Ochratoxin A, Patulin, and Trichothecenes have received particular attention due to their severe health outcomes in both humans and animals, which can range from acute to severe and chronic intoxications in both humans and animals (Ahn *et al.*, 2022; Nahle *et al.*, 2022).

Bouajila et al. (2022) reported that zearalenone contaminate feeds like corn, wheat, barley, sorghum, rice, and other grains have a variety of toxic effects on humans and animals (Jia *et al.*, 2022). Zearalenone (ZEN) is a potent non-steroidal oestrogen mycotoxin biosynthesized

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via the polyketide pathway and could bind to estrogen receptors, subsequently activating estrogen response elements in animals (Singh & Kumari, 2022; Yli-Mattila *et al.,* 2022).

Zearalenone (ZEN) consumption causes hypoestrogenism in animals and interferes with the expression of estrogen and organ function (Gajęcka *et al.,* 2021). It could reduce the nutritional value of feed, damage the growth and health of livestock and poultry, and cause huge economic losses to livestock production. However, some animals, like chickens, show strong resistance to the toxicity of ZEN. ZEN can also cause abortion, infertility, stillbirth, and other reproductive effects on animals (Yadav *et al.,* 2021; Jia *et al.,* 2022).

In humans, ZEN has a chronic toxicity effect and stimulates the growth of mammary gland cells that might be involved in breast cancer (Ropejko *et al.,* 2021). There is a report that shows ZEN has immunotoxin, hepatotoxic, hematotoxicity, and reproductive toxic effects like reducing fertility, vaginal prolapse, and causing vulvar swelling (Jia *et al.,* 2022). The degradation of zearalenone toxicity is commonly done by the use of physical, chemical, and biological approaches. Zearalenone is heat-stable and shows great resistance to conventional degradation methods (Kabak *et al.,* 2006; Wu *et al.,* 2021). However, physical and chemical degradation destroys nutritional structure, decreases palatability of the feed, and causes pollution to the environment (Guan *et al.,* 2021). Biological degradation has great specificity and degrades zearalenone completely without producing harmless products (Xu *et al.,* 2022).

Recently, numerous studies have focused on degradation through biological approaches by using microorganisms including bacteria, yeast, and fungi, and microorganisms' enzymes to remove zearalenone from food sources (Luo *et al.,* 2020; Nahle *et al.,* 2022). The development of genetic engineering technology in the advancement of recombinant proteins improves the enzymatic degradation of zearalenone (Guan *et al.,* 2021). This review aims to discuss the biological degradation of ZEN through microorganisms and enzymes developed in recent years.

2. Degradation of Zearalenone by Microorganisms

Microbial degradation occurs when microorganisms (bacterial and yeast) secrete their metabolites or enzymes during their growth and development process. Microorganisms can directly adsorb targeted toxins or reduce toxins of interest to impede the production of mycotoxins (Feng *et al.,* 2020; Xu *et al.,* 2022). Many studies have reported on the biodegradation of ZEN using microorganisms. They show high specificity and eco-friendliness in decreasing the possibility of ZEN toxicity from food and feed (Song *et al.,* 2021). A variety of non-pathogenic microbes like probiotics, *Bacillus*, *Saccharomyces*, and *Lactobacillus* species have a high capability to detoxify feeds contaminated with zearalenone because they follow standards like safe to be used and possess detoxifying ability without forming bad odour or taste in the feeds (Wang *et al.,* 2019; Zhu *et al.,* 2021).

Many studies reveal the detoxification of zearalenone using probiotics, including yeast, *Bacillus,* and lactic acid bacteria, as they are involved in the adsorption of ZEN and preventing its absorption by animals (Hathout & Aly, 2014). Various bacteria, yeasts, and fungi can convert ZEN to alpha and beta zearalenol (Cho *et al.,* 2010). Among *Bacillus* strains, *B. licheniformis, B. subtilis, B. natto,* and *B. cerues* were those found to have the highest detoxification effect on zearalenon in food and feed (Wang *et al.,* 2019). *Bacillus pumlius* ANSB01G is also reported to degrade ZEN in the feed of animals (Xu *et al.,* 2022). According to Xu *et al.* (2016) *B. amyloliquefaciens* ZDS-1 has ZEN degrading ability in screened colonies.

Probiotics are a great choice for biodegradation of ZEN in the food industry because it shows health benefits for humans and animals. Most lactic acid bacteria [LABs] are considered as safe probiotics in the food industry. It is reported that *Lactobacillus* strains have a potential role in degrading ZEN from fermented food products (Średnicka *et al.,* 2021). *Lact. paracasei*, and *Lc.*

lacti have the ability to remove ZEN in aqueous food solutions (Kabak *et al.*, 2006). There is a report that shows zearalenone can be degraded from PBS buffer solution by *Lact. acidophilus* CIP 76.13T by a bioremediation range of 57% (Ragoubi *et al.*, 2021).

There is a report that shows *B. licheniformis* CK1 has good probiotic properties and can degrade ZEN more than 90% after 36 hours of incubation in the contaminated corn meal medium by ZEN (Hsu *et al.*, 2018). Other strains of bacteria called *Saccharomyces cerevisiae* also have high ZEN degradation abilities as described in Table 1. There is a report that shows *S. cerevisiae* isolated from grapes can degrade ZEN (Rogowska *et al.*, 2019).

Saccharomyces cerevisiae isolated from silage has biodegradation properties and can degrade up to 90% of ZEN in two days (Keller *et al.*, 2015). According to Harkai *et al.* (2016) the bacteria *Streptomyces rimosus* (K145, K189) can degrade ZEN in liquid media. Wang et al. (2018) also investigated whether a *Lysinibacillus* strain isolated from chicken large intestine digest is capable of degrading zearalenone. Degradation of zearalenone by microorganism was illustrated in Table 1.

Table 1. *Recent research that shows microorganisms used for the degradation of zearalenone (ZEN).*

Food source or media used	Strain	ZEN concentration	Degradation range	References
Liquid LB medium	*Streptomyces rimosus* [K145, K189]	1 µg mL-1	100%	(Harkai *et al.*, 2016)
Feed	*Bacillus licheniformis* CK1	1.20 ± 0.11, 0.47 ± 0.22 mg/kg	Can degrade ZEN	(Fu *et al.*, 2016)
Liquid chromatography-tandem mass spectrometry and thin layer chromatography	*Candida parapsilosis*	20 µg/mL	Decreased by 97%	(Pan *et al.*, 2022)
Potassium phosphate buffer	*Lact. plantarum* 3QB361	2 µg/mL	82%	(Møller *et al.*, 2021)
Aqueous solution	*Lact. plantarum* BCC 47723	0.2 µg/mL	0.5%–23%	(Adunphatcharaphon *et al.*, 2021)
Culture medium/liquid food /solid-state fermentation	*Bacillus subtilis* *Bacillus natto*	20ug/mL, 1 mg/kg, 20 µg/mL	Culture mdium [100% and 87%], liquid food [65% and 73%], SSF [75% and 70%]	(Ju *et al.*, 2019)
Nutrient broth	*Bacillus subtilis, Candida utilis, Aspergillus oryzae*	1 µg/mL	[92.27- 95.15]%	(Liu *et al.*, 2019)
Malting wheat grains with bacterial suspension	*P. acidilactici*	19.5–873.7 µg/L	38.0%	(Juodeikiene *et al.*, 2018)
LB medium and simulated gastric fluid [GSF]	*Bacillus cereus* BC7	10 mg/L	100% and 89.31%	(Wang *et al.*, 2018)
Corn meal medium	*B. licheniformis* CK1	5 µg/mL	73%	(Hsu *et al.*, 2018)
Culture medium	*Bacillus pumilus* ES 21	17.9 mg/mL	95.7%	(Wang *et al.*, 2017)
MRS broth	*Lactobacillus rhamnosus*	200 µg/mL	Showed the highest adsorption [68.2%]	(Vega *et al.*, 2017)
MRS broth	*Lactobacillus plantarum* ZJ316	5 mg/L	highest ZEA degradation ability	(Chen *et al.*, 2018)
The LB medium	*Acinetobacter calcoaceticus*	5 µg/mL	85.77%	(Deng *et al.*, 2021)
HPLC-TOF-MS and NMR	*B. subtilis* Y816	40 mg/L	Transform of ZEN within 7 hour	(Bin *et al.*, 2021)
Cell suspensions on MRS agar	*Lb.fermentum* 2I3, *Lb.reuteri* L26, *Lb.plantarum* L81, *Lb.reuteri*, *Lb.plantarum* CCM 1904,	0.01 ppm	[57.9—100]%	(Harčárová *et al.*, 2022)
Cell suspensions on MRS agar	*Bacillus subtilis* CCM 2794	0.01 ppm	11.7 %	(Harčárová *et al.*, 2022)

3. Degradation of Zearalenone by Enzymes

Recent advancements in genetic engineering technology have attracted researchers' attention towards recombinant enzymes to degrade mycotoxins in food and feed with high efficiency. The attainment and cloning of recombinant enzyme genes lead to the safe expression of genes in microbes, which has become a novel progress in molecular modification for ZEN degradation (Azam *et al.*, 2019; Xu *et al.*, 2022).

Enzymatic degradation has wide advantages over microbial degradation because it can perform biodegradation with high efficiency, lower cost, reproducibility, and homogenous performance (Loi *et al.*, 2017; Liu *et al.*, 2022). A bacterial strain of *E. coli*, *S. cerevisiae*, and *Pichia pastoris* has been reported to remove ZEN from the culture medium (Wang *et al.*, 2020). Gao et al. (2022) identify and describe the activity of the ZEN degrading enzyme from *Exophiala spinifera*, ZHD_LD. Recently, microbial strains which can degrade ZEN have been isolated, and subsequently genes like ZHD101, ZLHY-6, and ZEN-jjm, as well as ZHD518 have been cloned (Cheng *et al.*, 2010). ZHD101 is one of the recombinant enzymes derived from *Clonostachys rosea* that degrades ZEN (Yang *et al.*, 2017). Wang et al. (2018) reported that the lactonohydrolase Zhd518 enzyme in *E. coli* has high biodegrading ability against ZEN in food and feed industries. A study that shows RmZHD, a ZEN hydrolyzing enzyme from *Rhinocladiella mackenziei*, has the ability to degrade ZEN (Zhou *et al.*, 2020).

Recombinant Prx (peroxiredoxin), a cloned gene from *Acinetobacter* sp. SM04 expressed in *E. coli*, has the ability to degrade ZEN in the presence of hydrogen peroxide (Yu *et al.*, 2012). It has been reported that laccase enzymes that are found in bacterial and yeast cells have the ability to degrade mycotoxins (Bi *et al.*, 2018). Song *et al.* (2021) show the laccase gene obtained from the fungus *P. pulmonarius* has an enzymatic property to degrade zearalenone when it is expressed in the *Pichia pastoris* X33 yeast strain by producing recombinant protein as shown in Table 2.

Studies have shown that laccase enzymes are considered as an effective zearalenone toxicity antidote. Furthermore, *Pleurotus eryngii* laccase enzyme can degrade aflatoxin B_1, ochratoxin A, zearalenon, and other mycotoxins (Wu *et al.*, 2021). A gene ZENC, zearalenone lactonase gene from *Neurospora crassa*, is expressed in *P. pastoris*. It had a maximal enzyme activity when fermented using high density fermatation at pH 8 and a temperature of 45 °C. Furthermore, ZENC was also found to be effective in ZEN containing feed materials with a high degradation rate (Guo *et al.*, 2020).

Garcia et al. (2018) also reported that the peroxidase enzyme has the ability to degrade zearalenone concentrations. According to the study, a fusion of multifunctional recombinant enzymes ZHDCP with genes of ZEN hydrolases and carboxypeptidases has the ability to detoxify zearalenone in 2 hours at pH and temperature of 35 °C (Azam *et al.*, 2019). The degradation of zearalenone by enzyme is discussed in (Table 2).

Table 2. *Enzymatic degradation of zearalenone (ZEN).*

Enzymes name	Source	Expression System	Degrading properties	References
Peroxiredoxin	*Acinetobacter* sp. SM04	*S. cerevisiae*	Optimal activity at pH 9.0, 80 ^{0}C and H_2O_2 concentration of 20 mmol/L Thermal stable, alkali resistance	(Tang *et al.*, 2013)
Lactone hydrolase ZHD	*Gliocladium roseum*	*P. pastoris*	Enzyme activity in flask fermentation was 22.5 U/mL and specific activity of 4976.5 U/mg· Maximum enzyme activity of the supernatant was 150.1 U/mL in 5-L fermenter	(Xiang *et al.*, 2016)
Cb ZHD	*C. rosea*	*Cladophialophora bantiana*	Optimal enzyme activity at temperature 35 °C and pH 8	(Hui *et al.*, 2017)
Lactonohydrolase	*Clonostachys rosea*	*Lactobacillus reuteri Pg4*	Not affect cell growth, acid and bile salt tolerance	(Yang *et al.*, 2017)
Lactonohydrolase Zhd518	*Clonostachys rosea*	*E. coli*	Activity of 207.0 U/mg with optimal temperature 40 ^{0}C and pH 8.	(Wang *et al.*, 2018)
Lactonase	*Neurospora crassa*	*P. pastoris*	Optimal activity at pH 8.0 and 45^{0}C, stable at pH 6.0–8.0 for 1 h at 37 ^{0}C, Maximal enzyme activity at 290.6 U/mL in 30-L fermenter	(Guo *et al.*, 2020)
Lactonehydrolase ZENC	*Neurospora crassa*	*P. pastoris*	99.75% of ZEN [20 µg/mL] was degraded at pH 8.0, 45 °C for 15 min	(Guo *et al.*, 2020)
Fusion ZHDCP enzyme	*C. rosea B.amyloliquefaciens* ASAG	*E. coli*	100% degradation rate at pH 7 and 30 ^{0}C	(Azam *et al.*, 2019)
ZLHY-6	*Pichia pastoris*	*P. pastoris* GSZ	low nutrient loss safe removal of ZEN	(Chang *et al.*, 2020)
lac2	*Pleurotus pulmonarius*	*P. pastoris* X33	Lac2-ABTS and Lac2-AS degrade ZEN at optimum pH 3.5 and temperature 55 ^{0}C of recombinant *Lac2*	(Song *et al.*, 2021)
Lactonohydrolase	*Trichoderma aggressivum*	*E. coli* BL21	With superior pH stability, the surface exhibit ZHD-P retained 80% activity	(Chen *et al.*, 2021)
ZPF1	*C. rosea* fused with *Phanerochaete chysosporium*	*Kluyveromyces lactis* GG799	ZEN degraded up to 46.21% ±3.17%	(Xia *et al.*, 2021)
DyP	*Streptomyces thermocarboxydus* 41291	*E. coli* BL21	ZEN was degraded slightly by StDyP	(Qin *et al.*, 2021)
Ase	*Acinetobacter* Sp	*E. coli* BL21	Degraded 88.4% of ZEN [20 µg/mL]	(Tang *et al.*, 2022)

3. CONCLUSION

The severe impact of zearalenone on animals and humans' health, present in contaminated food and feed, has received global attention. Many approaches have been established for the removal of ZEN. Biodegradation is considered the safest approach because it degrades toxins without residual toxic substances. Recent research shows the development of recombinant microorganisms and recombinant enzymes to detoxify ZEN in foods and feeds. However, the health impacts of recombinant enzymes are not clearly described. Currently, biodegradation of zearalenone is laboratory-based. The commercial scale of biodegradation needs further studies. Further interdisciplinary studies concerning gene cloning, genetic modification of microorganisms, and the development of recombinant enzymes are promising approaches for safe zearalenone degradation.

Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

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REFERENCES

Adunphatcharaphon, S., Petchkongkaew, A., & Visessanguan, W. (2021). *In vitro* mechanism assessment of zearalenone removal by plant-derived *Lactobacillus plantarum* BCC 47723. *Toxins*, *13*, 286. https://doi.org/10.3390/toxins13040286

Ahn, J.Y., Kim, J., Cheong, D.H., Hong, H., Jeong, J.Y., & Kim, B.G. (2022). An In Vitro Study on the Efficacy of Mycotoxin Sequestering Agents for Aflatoxin B1, Deoxynivalenol, and Zearalenone. *Animals*, *12*(3), 333. https://doi.org/10.3390/ani12030333

Arroyo-Manzanares, N., Campillo, N., López-García, I., Hernández-Córdoba, M., & Viñas, P. (2021). High-Resolution mass spectrometry for the determination of mycotoxins in biological samples. A review. *Microchemical Journal*, *166*, 106197. https://doi.org/10.1016/j.microc.2021.106197

Azam, M.S., Yu, D., Liu, N., & Wu, A. (2019). Degrading ochratoxin A and zearalenone mycotoxins using a multifunctional recombinant enzyme. *Toxins, 11*(5), 301. https://doi.org/10.3390/toxins11050301

Bergman, A., Wenning, L., Siewers, V., & Nielsen, J. (2018). Investigation of putative regulatory acetylation sites in Fas2p of *Saccharomyces cerevisiae*. *bioRxiv*, 430918. https://doi.org/10.1101/430918

Bi, K, Zhang, W., Xiao, Z., & Zhang. D. (2018). Characterization, expression and application of a zearalenone degrading enzyme from *Neurospora crassa*. *AMB Express*, *8*, 194. https://doi.org/10.1186/s13568-018-0723-z

Bin, Y.S., Zheng, H.C., Xu, J.Y., Zhao, X.Y., Shu, W.J., Li, X.M., Song, H., & Ma, Y.H. (2021). New biotransformation mode of zearalenone identifed in *Bacillus subtilis* Y816 revealing a novel ZEN conjugate. *Journal of Agricultural and Food Chemistry*, *69*(26), 7409–7419. https://doi.org/10.1021/acs.jafc.1c01817

Bouajila, A., Lamine, M., Hamdi, Z., Ghorbel, A., & Gangashetty, P. (2022). A Nutritional Survey of Local Barley Populations Based on the Mineral Bioavailability, Fatty Acid Profile, and Geographic Distribution of *Fusarium* Species and the Mycotoxin Zearalenone (ZEN). *Agronomy*, *12*(4), 916. https://doi.org/10.3390/agronomy12040916

Chang, X., Liu, H., Sun, J., Wang, J., Zhao, C., Zhang, W., Zhang, J., & Sun, C. (2020). Zearalenone removal from corn oil by an enzymatic strategy. *Toxins (basel)*, *12*, 1–14. https://doi.org/10.3390/toxins12020117

Chen, S., Pan, L., Liu, S., Pan, L., Li, X., & Wang, B. (2021). Recombinant expression and surface display of a zearalenone lactonohydrolase from Trichoderma aggressivum in *Escherichia coli*. *Protein Expression and Purification, 187*, 105933. https://doi.org/10.1016/j.pep.2021.105933

Chen, S.W., Hsu, J.T., Y.-A. Chou, Y.A., & Wang, H.T. (2018). The application of digestive tract lactic acid bacteria with high esterase activity for zearalenone detoxification. *Journal of the Science of Food and Agriculture, 98*(10), 3870-3879. https://doi.org/10.1002/jsfa.8904

Cheng, B., Shi, W., Luo, J., Peng, F., Wan, C., & Wei, H. (2010). Cloning of zearalenone-degraded enzyme gene (ZEN-jjm) and its expression and activity analysis. *Journal of Agricultural Biotechnology, 18*(2), 225-230. https://doi.org/10.3969/j.issn.1674-7968.2010.02.004

Cho, K.J., Kang, J.S., Cho, W.T., Lee, C.H., Ha, J.K., & Song, K.B. (2010). In vitro degradation of zearalenone by *Bacillus subtilis*. *Biotechnology Letters, 32*(12), 1921-1924. https://doi.org/10.1007/s10529-010-0373-y

Deng, T., Yuan, Q.S., Zhou, T., Guo, L.P., Jiang, W.K., Zhou, S.H., Yang, C.G., & Kang, C.Z. (2021). Screening of zearalenone-degrading bacteria and analysis of degradation conditions. *China Journal of Chinese Materia Medica, 46*(20), 5240-5246. https://doi.org/10.19540/j.cnki.cjcmm.20210716.101

Feng, Y., Huang, Y., Zhan, H., Bhatt, P., & Chen, S. (2020). An overview of strobilurin fungicide degradation: current status and future perspective. *Frontiers in Microbiology, 11*, 389. https://doi.org/10.3389/fmicb.2020.00389

Fu, G., Ma, J., Wang, L., Yang, X., Liu, J., & Zhao, X. (2016). Effect of degradation of zearalenone-contaminated feed by *Bacillus licheniformis* CK1 on postweaning female piglets. *Toxins, 8*(10), 300. https://doi.org/10.3390/toxins8100300

Gajęcka, M., Majewski, M.S., Zielonka, Ł., Grzegorzewski, W., Onyszek, E., Lisieska-Żołnierczyk, S., Juśkiewicz, J., Babuchowski, A., & Gajęcki, M.T. (2021). Concentration of Zearalenone, Alpha-Zearalenol and Beta-Zearalenol in the Myocardium and the Results of Isometric Analyses of the Coronary Artery in Prepubertal Gilts. *Toxins, 13*(6), 396. https://doi.org/10.3390/toxins13060396

Gao, D., Cao, X., Ren, H., Wu, L., Yan, Y., Hua, R., Xing, W., Lei, M., & Liu, J. (2022). Immunotoxicity and uterine transcriptome analysis of the effect of zearalenone (ZEA) in sows during the embryo attachment period. *Toxicology Letters, 357*, 33-42. https://doi.org/10.1016/j.toxlet.2021.12.017

Garcia, S.O., Feltrin, A.C.P., & Garda-Buffon, J. (2018). Zearalenone reduction by commercial peroxidase enzyme and peroxidases from soybean bran and rice bran. *Food Additives & Contaminants*: Part A, *35*(9), 1819-1831. https://doi.org/10.1080/19440049.2018.1486044

Greeff-Laubscher, M.R., Beukes, I., Marais, G.J., & Jacobs, K. (2020). Mycotoxin production by three different toxigenic fungi genera on formulated abalone feed and the effect of an aquatic environment on fumonisins. *Mycology, 11*(2), 105-117. https://doi.org/10.1080/21501203.2019.1604575

Guan, Y., Chen, J., Nepovimova, E., Long, M., Wu, W., & Kuca, K. (2021). Aflatoxin detoxification using microorganisms and enzymes. *Toxins, 13*(1), 46. https://doi.org/10.3390/toxins13010046

Guo, Y., Qin, X., Tang, Y., Ma, Q., Zhang, J., & Zhao, L. (2020). CotA laccase, a novel aflatoxin oxidase from Bacillus licheniformis, transforms aflatoxin B1 to aflatoxin Q1 and epi-aflatoxin Q1. *Food Chemistry, 325*, 126877. https://doi.org/10.1016/j.foodchem.2020.126877

Harčárová, M., Čonková, E., Naď, P., & Proškovcová, M. (2022). Zearalenone Biodegradation by the Spp. and Spp. *Folia Veterinaria, 66*(1), 70-74. https://doi.org/10.2478/fv-2022-0008

Harkai, P., Szabó, I., Cserháti, M., Krifaton, C., Risa, A., Radó, J., Balázs, A., Berta, K., & Kriszt, B. (2016). Biodegradation of aflatoxin-B1 and zearalenone by Streptomyces sp. collection. *International Biodeterioration & Biodegradation, 108*, 48-56. https://doi.org/10.1016/j.ibiod.2015.12.007

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

Hsu, T.C., Yi, P.J., Lee, T.Y., & Liu, J.R. (2018). Probiotic characteristics and zearalenone-removal ability of a Bacillus licheniformis strain. *PloS One, 13*(4), e0194866. https://doi.org/10.1371/journal.pone.0194866

Hui, R., Hu, X., Liu, W., Liu, W., Zheng, Y., Chen, Y., Guo, R.-T., Jin, J., & Chen, C.-C. (2017). Characterization and crystal structure of a novel zearalenone hydrolase fromCladophialophora bantiana. *Acta Crystallographica Section F Structural Biology Communications, 73*(9), 515–519. https://doi.org/10.1107/s2053230x17011840

Jia, S., Ren, C., Yang, P., & Qi, D. (2022). Effects of Intestinal Microorganisms on Metabolism and Toxicity Mitigation of Zearalenone in Broilers. *Animals, 12*(15), 1962. https://doi.org/10.3390/ani12151962

Ju, J., Tinyiro, S.E., Yao, W., Yu, H., Guo, Y., Qian, H., & Xie, Y. (2019). The ability of Bacillus subtilis and Bacillus natto to degrade zearalenone and its application in food. *Journal of Food Processing and Preservation, 43*(10), e14122. https://doi.org/10.1111/jfpp.14122

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

Kabak, B., Dobson, A.D., & Var, I.I.L. (2006). Strategies to prevent mycotoxin contamination of food and animal feed: a review. *Critical reviews in food science and nutrition, 46*(8), 593-619. https://doi.org/10.1080/10408390500436185

Keller, L., Abrunhosa, L., Keller, K., Rosa, C.A., Cavaglieri, L., & Venâncio, A. (2015). Zearalenone and its derivatives α-zearalenol and β-zearalenol decontamination by Saccharomyces cerevisiae strains isolated from bovine forage. *Toxins, 7*(8), 3297-3308. https://doi.org/10.3390/toxins7083297

Li, S.J., Zhang, G., Xue, B., Ding, Q., Han, L., Huang, J.C., Wu, F., Li, C., & Yang, C. (2022). Toxicity and detoxification of T-2 toxin in poultry. *Food and Chemical Toxicology*, 113392. https://doi.org/10.1016/j.fct.2022.113392

Liu, C., Chang, J., Wang, P., Yin, Q., Huang, W., Dang, X., Lu, F., & Gao, T. (2019). Zearalenone biodegradation by the combination of probiotics with cell-free extracts of *Aspergillus* oryzae and its mycotoxin-alleviating effect on pig production performance. *Toxins, 11*(10), 552. https://doi.org/10.3390/toxins11100552

Liu, L., Xie, M., & Wei, D. (2022). Biological Detoxification of Mycotoxins: Current Status and Future Advances. *International Journal of Molecular Sciences, 23*(3), 1064. https://doi.org/10.3390/ijms23031064

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

Luo, Y., Liu, X., Yuan, L., & Li, J. (2020). Complicated interactions between bio-adsorbents and mycotoxins during mycotoxin adsorption: Current research and future prospects. *Trends in Food Science & Technology, 96*, 127-134. https://doi.org/10.1016/j.tifs.2019.12.012

Møller, C.O. de A., Freire, L., Rosim, R.E., Margalho, L.P., Balthazar, C.F., Franco, L.T., Sant'Ana, A. de S., Corassin, C.H., Rattray, F.P., & Oliveira, C.A.F. de. (2021). Effect of Lactic Acid Bacteria Strains on the Growth and Aflatoxin Production Potential of

Aspergillus parasiticus, and Their Ability to Bind Aflatoxin B1, Ochratoxin A, and Zearalenone in vitro. *Frontiers in Microbiology*, *12*. https://doi.org/10.3389/fmicb.2021.655386

Nahle, S., El Khoury, A., Savvaidis, I., Chokr, A., Louka, N., & Atoui, A. (2022). Detoxification approaches of mycotoxins: by microorganisms, biofilms and enzymes. *International Journal of Food Contamination*, *9*(1), 1-14. https://doi.org/10.1186/s40550-022-00089-2

Navale, V.D., & Vamkudoth, K. (2022). Toxicity and preventive approaches of *Fusarium* derived mycotoxins using lactic acid bacteria: state of the art. *Biotechnology Letters*, 1-16. https://doi.org/10.1007/s10529-022-03293-4

Pan, Y., Liu, C., Yang, J., & Tang, Y. (2022). Conversion of zearalenone to β-zearalenol and zearalenone-14, 16-diglucoside by Candida parapsilosis ATCC 7330. *Food Control*, *131*, 108429. https://doi.org/10.1016/j.foodcont.2021.108429

Qin, X., Xin, Y., Su, X., Wang, X., Wang, Y., Zhang, J., Tu, T., Yao, B., Luo, H., & Huang, H. (2021). Efficient degradation of zearalenone by dyedecolorizing peroxidase from *streptomyces thermocarboxydus* combining catalytic properties of manganese peroxidase and laccase. *Toxins (Basel) 13*, 602. https://doi.org/10.3390/toxins13090602

Ragoubi, C., Quintieri, L., Greco, D., Mehrez, A., Maatouk, I., D'Ascanio, V., Landoulsi, A., & Avantaggiato, G. (2021). Mycotoxin removal by Lactobacillus spp. and their application in animal liquid feed. *Toxins, 13*(3), 185. https://doi.org/10.3390/toxins13030185

Rogowska, A., Pomastowski, P., Sagandykova, G., & Buszewski, B. (2019). Zearalenone and its metabolites: Effect on human health, metabolism and neutralisation methods. *Toxicon, 162*, 46-56. https://doi.org/10.1016/j.toxicon.2019.03.004

Ropejko, K., & Twarużek, M. (2021). Zearalenone and its metabolites—general overview, occurrence, and toxicity. *Toxins, 13*(1), 35. https://doi.org/10.3390/toxins13010035

Singh, K., & Kumari, A. (2022). Traditional Mycotoxins and Their Health Implications. *Mycotoxins and Mycotoxicoses*, 27-64. https://doi.org/10.1007/978-981-19-2370-8_3

Song, Y., Wang, Y., Guo, Y., Qiao, Y., Ma, Q., Ji, C., & Zhao, L. (2021). Degradation of zearalenone and aflatoxin B1 by Lac2 from Pleurotus pulmonarius in the presence of mediators. *Toxicon, 201*, 1-8. https://doi.org/10.1016/j.toxicon.2021.08.003

Średnicka, P., Juszczuk-Kubiak, E., Wójcicki, M., Akimowicz, M., & Roszko, M. (2021). Probiotics as a biological detoxification tool of food chemical contamination: A review. *Food and Chemical Toxicology, 153*, 112306. https://doi.org/10.1016/j.fct.2021.112306

Tang, Y., Liu, C., Yang, J., & Peng, X. (2022). A novel enzyme synthesized by *Acinetobacter* sp. SM04 is responsible for zearalenone biodegradation. *Bioscience, Biotechnology, and Biochemistry*, *86*, 209–216. https://doi.org/10.1093/bbb/zbab204

Tang, Y., Xiao, J., Chen, Y., Yu, Y., Xiao, X., Yu, Y., & Wu, H. (2013). Secretory expression and characterization of a novel peroxiredoxin for zearalenone detoxification in Saccharomyces cerevisiae. *Microbiological Research*, *168*(1), 6-11. https://doi.org/10.1016/j.micres.2012.08.002

Vega, M.F., Dieguez, S.N., Riccio, B., Aranguren, S., Giordano, A., Denzoin, L., Soraci, A.L., Tapia, M.O., Ross, R., Apás, A., & González, S.N. (2017). Zearalenone adsorption capacity of lactic acid bacteria isolated from pigs. *Brazilian Journal of Microbiology, 48*, 715-723. https://doi.org/10.1016/j.bjm.2017.05.001

Wang, G., Yu, M., Dong, F., Shi, J., & Xu, J. (2017). Esterase activity inspired selection and characterization of zearalenone degrading bacteria *Bacillus pumilus* ES-21. *Food Control, 77*, 57-64. https://doi.org/10.1016/j.foodcont.2017.01.021

Wang, J., & Xie, Y. (2020). Review on microbial degradation of zearalenone and aflatoxins. *Grain & Oil Science and Technology, 3*(3), 117-125. http://dx.doi.org/10.1016/j.gaost.2020.05.002

Wang, J.Q., Yang, F., Yang, P.L., Liu, J., & Lv, Z.H. (2018). Microbial reduction of zearalenone by a new isolated *Lysinibacillus* sp. ZJ-2016-1. *World Mycotoxin Journal, 11*(4), 571-578. https://doi.org/10.3920/WMJ2017.2264

Wang, M., Yin, L., Hu, H., Selvaraj, J.N., Zhou, Y., & Zhang, G. (2018). Expression, functional analysis and mutation of a novel neutral zearalenone-degrading enzyme. *International Journal of Biological Macromolecules, 118*, 1284-1292. https://doi.org/10.1016/j.ijbiomac.2018.06.111

Wang, N., Wu, W., Pan, J., & Long, M. (2019). Detoxification strategies for zearalenone using microorganisms: A review. *Microorganisms*, *7*(7), 208. https://doi.org/10.3390/microorganisms7070208

Wang, Y., Wang, G., Dai, Y., Wang, Y., Lee, Y.W., Shi, J., & Xu, J. (2020). Biodegradation of deoxynivalenol by a novel microbial consortium. *Frontiers in Microbiology*, *10*, 2964. https://doi.org/10.3389/fmicb.2019.02964

Wang, Y., Zhang, J., Wang, Y., Wang, K., Wei, H., & Shen, L. (2018). Isolation and characterization of the Bacillus cereus BC7 strain, which is capable of zearalenone removal and intestinal flora modulation in mice. *Toxicon, 155*, 9-20. https://doi.org/10.1016/j.toxicon.2018.09.005

Wu, N., Ou, W., Zhang, Z., Wang, Y., Xu, Q., & Huang, H. (2021). Recent advances in detoxification strategies for zearalenone contamination in food and feed. *Chinese Journal of Chemical Engineering*, *30*, 168-177. https://doi.org/10.1016/j.cjche.2020.11.011

Xia, Y., Wu, Z., He, R., Gao, Y., Qiu, Y., Cheng, Q., Ma, X., & Wang, Z. (2021). Simultaneous degradation of two mycotoxins enabled by a fusion enzyme in food-grade recombinant Kluyveromyces lactis. *Bioresources and Bioprocessing*, *8*(1). https://doi.org/10.1186/s40643-021-00395-1

Xiang, L., Wang, Q., Zhou, Y., Yin, L., Zhang, G., & Ma, Y. (2016). High-level expression of a ZEN-detoxifying gene by codon optimization and biobrick in Pichia pastoris. *Microbiological Research, 193*, 48–56. https://doi.org/10.1016/j.micres.2016.09.004

Xu, H., Wang, L., Sun, J., Wang, L., Guo, H., Ye, Y., & Sun, X. (2022). Microbial detoxification of mycotoxins in food and feed. *Critical Reviews in Food Science and Nutrition*, *62*(18), 4951-4969. https://doi.org/10.1080/10408398.2021.1879730

Xu, J., Wang, H., Zhu, Z., Ji, F., Yin, X., Hong, Q., & Shi, J. (2016). Isolation and characterization of Bacillus amyloliquefaciens ZDS-1: Exploring the degradation of Zearalenone by Bacillus spp. *Food Control*, *68*, 244-250. https://doi.org/10.1016/j.foodcont.2016.03.030

Xu, L., Sun, X., Wan, X., Li, H., Yan, F., Han, R., Li, H., Li, Z., Tian, Y., Liu, X., & Kang, X. (2020). Identification of a Bacillus amyloliquefaciens H6 thioesterase involved in zearalenone detoxification by transcriptomic analysis. *Journal of Agricultural and Food Chemistry*, *68*(37), 10071-10080. https://doi.org/10.1021/acs.jafc.0c03954

Yadav, R., Yadav, P., Singh, G., Kumar, S., Dutt, R., & Pandey, A.K., (2021). Non-infectious Causes of Abortion in Livestock Animals-A. *International Journal of Livestock Research, 11*(2), 1-13. https://doi.org/10.5455/ijlr.20201031015650

Yang, S.B., Zheng, H.C., Xu, J.Y., Zhao, X.Y., Shu, W.J., Li, X.M., Song, H., & Ma, Y.H. (2021). New biotransformation mode of zearalenone identified in Bacillus subtilis Y816 revealing a novel ZEN conjugate. *Journal of Agricultural and Food Chemistry*, *69*(26), 7409-7419. https://doi.org/10.1021/acs.jafc.1c01817

Yang, W.C., Hsu, T.C., Cheng, K.C., & Liu, J.R. (2017). Expression of the Clonostachys rosea lactonohydrolase gene by Lactobacillus reuteri to increase its zearalenone-removing ability. *Microbial Cell Factories*, *16*(1), 1-11. https://doi.org/10.1186/s12934-017-0687-8

Yli-Mattila, T., Yörü, E., Abbas, A., & Teker, T. (2022). Overview on Major Mycotoxins Accumulated on Food and Feed. *Fungal Biotechnology Prospects and Avenues*, 310–343. https://doi.org/10.1201/9781003248316-16

Yu, Y., Wu, H., Tang, Y., & Qiu, L. (2012). Cloning, expression of a peroxiredoxin gene from Acinetobacter sp. SM04 and characterization of its recombinant protein for zearalenone detoxification. *Microbiological Research*, *167*(3), 121-126. https://doi.org/10.1016/j.micres.2011.07.004

Zhou, J., Zhu, L., Chen, J., Wang, W., Zhang, R., Li, Y., Zhang, Q., & Wang, W. (2020). Degradation mechanism for Zearalenone ring-cleavage by Zearalenone hydrolase RmZHD: A QM/MM study. *Science of the Total Environment*, *709*, 135897. https://doi.org/10.1016/J.SCITOTENV.2019.135897

Zhu, Y., Drouin, P., Lepp, D., Li, X.Z., Zhu, H., Castex, M., & Zhou, T. (2021). A Novel Microbial Zearalenone Transformation through Phosphorylation. *Toxins*, *13*(5), 294. https://doi.org/10.3390/toxins13050294