

Degradation of zearalenone by microorganisms and enzymes

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ABSTRACT

Mycotoxins are toxic metabolites produced by fungi that may cause serious health problems in humans and animals. Zearalenone is a secondary metabolite produced by fungi of the genus *Fusarium*, widely exists in animal feed and human food. One concern with the use of microbial strains and their enzyme derivatives for zearalenone degradation is the potential variability in the effectiveness of the degradation process. The efficiency of degradation may depend on various factors such as the type and concentration of zearalenone, the properties of the microbial strains and enzymes, and the environmental conditions. Therefore, it is important to carefully evaluate the efficacy of these methods under different conditions and ensure their reproducibility. Another important consideration is the safety and potential side effects of using microbial strains and enzymes for zearalenone degradation. It is necessary to evaluate the potential risks associated with the use of genetically modified microorganisms or recombinant enzymes, including their potential impact on the environment and non-target organisms. Additionally, it is important to ensure that the degradation products are indeed harmless and do not pose any health risks to humans or animals. Furthermore, while the use of microbial strains and enzymes may offer an environmentally friendly and cost-effective solution for zearalenone degradation, it is important to explore other methods such as physical or chemical treatments as well. These methods may offer complementary approaches for zearalenone detoxification, and their combination with microbial or enzyme-based methods may improve overall efficacy. Overall, the research on the biodegradation of zearalenone using microorganisms and enzyme derivatives is promising, but there are important considerations that need to be addressed to ensure the safety and effectiveness of these methods. Development of recombinant enzymes improves enzymatic detoxification of zearalenone to a non-toxic product without damaging the nutritional content. This review summarizes biodegradation of zearalenone using microorganisms and enzyme derivatives to nontoxic products. Further research is needed to fully evaluate the potential of these methods for mitigating the impact of mycotoxins in food and feed.

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INTRODUCTION

Mycotoxins are naturally occurring toxic secondary metabolites of some microscopic filamentous fungi (Liu, Xie & Wei, 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). Zearalenone is an estrogenic mycotoxin produced by *Fusarium* species that leads to huge economic losses in the food industry and livestock husbandry. About 25–50% of the world's food crops are affected by mycotoxins (Eskola *et al.*, 2020). The most economically important mycotoxins are aflatoxins, deoxynivalenol and zearalenone. Contamination of food and feed with zearalenone has reproductive problems, carcinogenicity, immunotoxicity, and other cytotoxic effects (Ropejko & Twaruzek, 2021; Yli-Mattila *et al.*, 2022).

More than 400 different types of mycotoxins have been identified so far, with different levels of toxicity (Arroyo-Manzanares *et al.*, 2021). Among mycotoxins, aflatoxins B1, zearalenone, ochratoxin A, patulin, and trichothecenes have received particular attention due to their severe health outcomes on 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 have a variety of toxic effects on humans and animals (Jia *et al.*, 2022). Zearalenone (ZEN) is a potent non-steroidal oestrogen mycotoxin which is biosynthesized *via* the polyketide pathway and could bind to estrogen receptors, which subsequently activate estrogen response elements in animals (Singh & Kumari, 2022; Yli-Mattila *et al.*, 2022).

Zearalenone (ZEN) consumption causes hypoestrogenism in animals and interferes in the expression of estrogen and organ function (Gajecka *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 & Twaruzek, 2021). There is a report that shows ZEN has immunotoxin, hepatotoxic, hematotoxic, and reproductive toxic effects like reducing fertility, vaginal prolapse, and causing vulvar swelling. The two primary metabolites of zearalenone are α -zearalenol (α -ZEL), which is a synthetic version of zearalenone, and β -zearalenol (β -ZEL), which is produced by reducing ZEN. Zearalenone is metabolized in the intestinal cells. Zearalenone also comes in the forms of α -zearalanol (α -ZAL) and β -zearalanol (β -ZAL). It is capable of being conjugated with glucuronic acid in its metabolized state (Ropejko & Twaruzek, 2021). 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, Dobson & Var, 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).

At present, microorganisms and enzymes derived from microbial strains have been widely used for the degradation of zearalenone in food and feed (Nahle *et al.*, 2022; Xu *et al.*, 2022). Researchers have developed biodegradation of zearalenone by the use of microbial and their enzyme derivatives, which offers harmless products and is environmentally friendly. 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). Development of genetic engineering technology in the advancement of recombinant proteins improves 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.

SURVEY METHODOLOGY

The varieties of mycotoxin-degrading microorganisms and enzymes, the development of heterologously generated degrading enzymes through genetic engineering, and related studies on enhancing the efficacy of degrading enzymes were all summarized in this review. The published articles were gathered using the databases Science Direct, Scopus, PubMed Web of Science, and a Gray literature resource like Google Scholar. The following keywords were used to search for the review: [Zearalenone Degradation OR Microorganisms OR Enzyme] and [zearalenone]. After passing the abstract screening, the full text of the found publications was downloaded. Any manuscript that wasn't available in this regard was discarded. For data extraction and analysis, only the articles with accessible full texts underwent further screening.

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 our 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 (Table 1). 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 odor or taste in the feeds (Wang *et al.*, 2019; Zhu *et al.*, 2021). Several studies reveal detoxification of zearalenone using probiotics, including by yeast, *Bacillus*, and lactic acid bacteria (Table 1) as they are involved in adsorption of ZEN and preventing its absorption by animals (Hathout & Aly, 2014).

Various bacteria, yeasts, and fungi can convert structure of ZEN to alpha and beta zearalenol through hydrolysis, conjugation of sulfate and glucosyl group reduction (Cho *et al.*, 2010). Among *Bacillus* strains, *B. licheniformis*, *B. subtilis*, *B. natto*, and *B. cereus* were those found to have the highest detoxification effect on zearalenone in food and feed (Wang

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	<i>Streptomyces rimosus</i> (K145, K189)	1 µg mL ⁻¹	100%	<i>Harkai et al. (2016)</i>
Feed	<i>Bacillus licheniformis</i> CK1	1.20 ± 0.11, 0.47 ± 0.22 mg/kg	Can degrade ZEN	<i>Fu et al. (2016)</i>
Liquid chromatography-tandem mass spectrometry and Thin layer chromatography	<i>Candida parapsilosis</i>	20 µg/mL	Decreased by 97%	<i>Pan et al. (2022)</i>
Potassium phosphate buffer	<i>Lact. plantarum</i> 3QB361	2 µg/mL	82%	<i>Møller et al. (2021)</i>
Aqueous solution	<i>Lact. plantarum</i> BCC 47723	0.2 µg/mL	0.5%–23%	<i>Adunphatcharaphon, Petchkongkaew & Visessanguan (2021)</i>
Culture medium/liquid food/solid-state fermentation	<i>Bacillus subtilis</i> <i>Bacillus natto</i>	20 µg/mL; 1 mg/kg; 20 µg/mL	100% and 87% 65, 73%/75%, 70%	<i>Ju et al. (2019)</i>
Nutrient broth	<i>Bacillus subtilis</i> , <i>Candida utilis</i> , <i>Aspergillus oryzae</i>	1 µg/mL	92.27% <i>A. oryzae</i> . combined form can degrade 95.15%	<i>Liu et al. (2019)</i>
Malting wheat grains with bacterial suspension	<i>P. acidilactici</i>	19.5–873.7 µg/L	38.0%	<i>Juodeikiene et al. (2018)</i>
LB medium and simulated gastric fluid (GSF)	<i>Bacillus cereus</i> BC7	10 mg/L	100% and 89.31%	<i>Wang et al. (2018)</i>
Corn meal medium	<i>B. licheniformis</i> CK1	5 µg/mL	73%	<i>Hsu et al. (2018)</i>
Culture medium	<i>Bacillus pumilus</i> ES 21	17.9 mg/ml	95.7%	<i>Wang et al. (2017)</i>
MRS broth	<i>Lactobacillus rhamnosus</i>	200 µg/mL	Showed the highest adsorption (68.2%)	<i>Vega et al. (2017)</i>
MRS broth	<i>Lactobacillus plantarum</i> ZJ316	5 mg/L	highest ZEA degradation ability	<i>Chen et al. (2018)</i>
The LB medium	<i>Acinetobacter calcoaceticus</i>	5 µg/mL	85.77%	<i>Deng et al. (2021)</i>

(continued on next page)

Table 1 (continued)

Food source or media used	Strain	ZEN concentration	Degradation range	References
HPLC-TOF-MS and NMR	<i>B. subtilis</i> Y816	40 mg/L	Transform of ZEN within 7 h	<i>Bin et al. (2021)</i>
Cell suspensions on MRS agar	<i>Lb.fermentum</i> 2I3, <i>Lb.reuteri</i> L26, <i>Lb.plantarum</i> L81, <i>Lb.reuteri</i> , <i>Lb.plantarum</i> CCM 1904,	0.01 ppm	(57.9—100)%	<i>Harčárová et al. (2022)</i>
Cell suspensions on MRS agar	<i>Bacillus subtilis</i> CCM 2794	0.01 ppm	11.7%	<i>Harčárová et al. (2022)</i>

et al., 2019). *Bacillus pumilus* 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 is 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 safe probiotics in the food industry. It is reported that *Lactobacillus* strains have a potential role in degrading ZEN from fermented food products (*Šrednicka et al., 2021*). *Lact. paracasei*, and *Lc. lacti* have the ability to remove ZEN in aqueous food solutions (*Wu et al., 2021*). 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 by more than 90% after 36 h of incubation in the contaminated corn meal medium by ZEN (*Hsu et al., 2018*). Other strains of fungi called *Saccharomyces cerevisiae* also have high ZEN degradation abilities. There is a report that shows *S. cerevisiae* isolate from grape 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 a *Lysinibacillus* strain isolated from chicken's large intestine digesta is capable of degrading zearalenone. Diagrammatic pathway for the process of degradation of zearalenone by microorganism (*Fig. 1*) source (*Mukherjee et al., 2014*).

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 leads 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, Xie & Wei, 2022*).

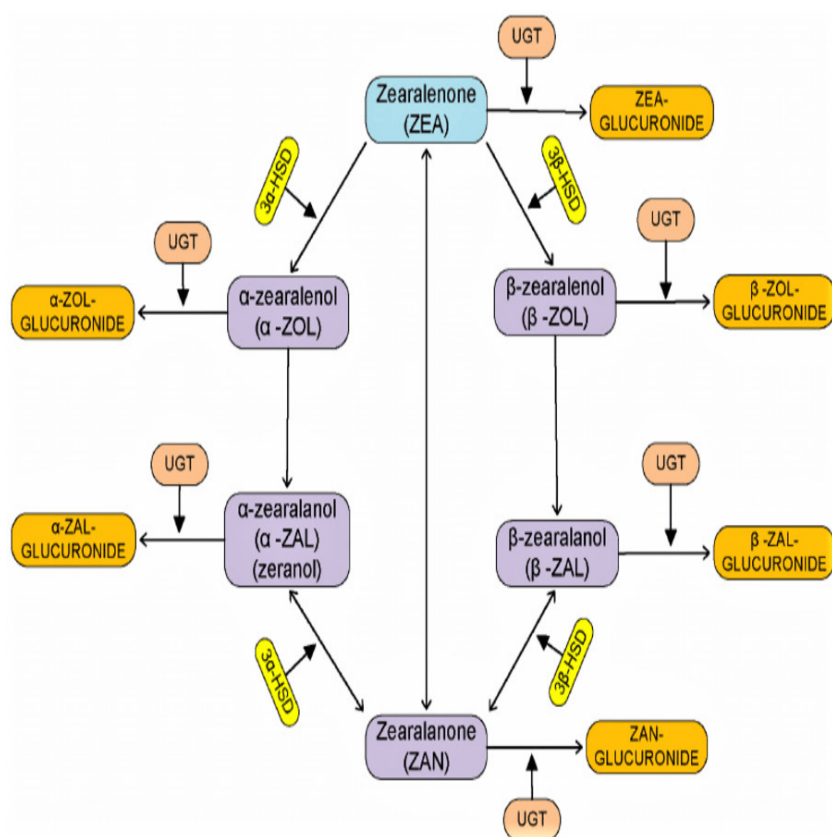


Figure 1 Diagrammatic pathway for the process of degradation of zearalenone by microorganism.

Full-size [DOI: 10.7717/peerj.15808/fig-1](https://doi.org/10.7717/peerj.15808/fig-1)

A bacterial strain of *E. coli*, *S. cerevisiae*, and *Pichia pastoris* has been reported to remove ZEN from culture medium (Wang & Xie, 2020). Gao et al. (2022) identify and describe the activity of the ZEN degrading enzyme from *Exophiala spinifera*, ZHD_LD. Recently, microbial strains that are able to 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. There is a study that shows RmZHD, a ZEN hydrolyzing enzyme from *Rhinochadiella 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 on bacterial and yeast cells have the ability to degrade mycotoxins (Guo et al., 2020). Song et al. (2021) show the laccase gene obtained from the fungus *P. pulmonarius* has an enzymatic property to degrade zearalenone when it was expressed in the *Pichia pastoris* X33 yeast strain by producing recombinant protein.

Table 2 Enzymatic degradation of zearalenone (ZEN).

Enzymes name	Source	Expression System	Degrading properties	References
Peroxiredoxin	<i>Acinetobacter</i> sp. SM04	<i>S. cerevisiae</i>	Optimal activity at pH 9.0, 80 °C and H ₂ O ₂ concentration of 20 mmol/L Thermal stable, alkali resistance	Tang et al. (2013)
Lactone hydrolase ZHD	<i>Gliocladium roseum</i>	<i>P. pastoris</i>	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	<i>C. rosea</i>	<i>Cladophialophora bantiana</i>	Optimal enzyme activity at temperature 35 °C and pH 8	Hui et al. (2017)
Lactonohydrolase	<i>Clonostachys rosea</i>	<i>Lactobacillus reuteri</i> Pg4	Not affect cell growth, acid and bile salt tolerance	Yang et al. (2017)
Lactonohydrolase Zhd518	<i>Clonostachys rosea</i>	<i>E. coli</i>	Activity of 207.0 U/mg with optimal temperature 40 °C and pH 8.	Wang et al. (2018)
Lactonase	<i>Neurospora crassa</i>	<i>P. pastoris</i>	Optimal activity at pH 8.0 and 45 °C, stable at pH 6.0–8.0 for 1 h at 37 °C, Maximal enzyme activity at 290.6 U/mL in 30-L fermenter	Bi et al. (2018)
Lactonehydrolase ZENC	<i>Neurospora crassa</i>	<i>P. pastoris</i>	99.75% of ZEN (20 µg/ml) was degraded at pH 8.0, 45 °C for 15 min	Bi et al. (2018)
Fusion ZHD/CP enzyme ZLHY-6	<i>C. rosea</i> <i>B.amyloliquefaciens</i> ASAG	<i>E. coli</i>	100% degradation rate at pH 7 and 30 °C	Azam et al. (2019)
<i>lac2</i>	<i>Pleurotus pulmonarius</i>	<i>P. pastoris</i> GSZ	low nutrient loss safe removal of ZEN	Chang et al. (2020)
<i>lac2</i>	<i>Pleurotus pulmonarius</i>	<i>P. pastoris</i> X33	Lac2-ABTS and Lac2-AS degrade ZEN at optimum pH 3.5 and temperature 55 °C of recombinant <i>Lac2</i>	Song et al. (2021)
Lactonohydrolase	<i>Trichoderma aggressivum</i>	<i>E. coli</i> BL21	With superior pH stability, the surface exhibit ZHD-P retained 80% activity	Chen et al. (2021)
ZPF1	<i>C. rosea</i> fused with <i>Phanerochaete chysosporium</i>	<i>Kluyveromyces lactis</i> GG799	ZEN degraded up to 46.21% ± 3.17%	Xia et al. (2021)
DyP	<i>Streptomyces thermocarboxydus</i> 41291	<i>E. coli</i> BL21	ZEN was degraded slightly by StDyP	Qin et al. (2021)
Ase	<i>Acinetobacter</i> Sp	<i>E. coli</i> BL21	Degraded 88.4% of ZEN (20 µg/mL)	Tang et al. (2022)

Studies have shown that laccase enzymes are considered to be an effective zearalenone toxicity antidote. Furthermore, *Pleurotus eryngii* laccase enzyme can degrade aflatoxin B1, ochratoxin A, zearalenone, 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 fermentation 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 (Bi et al., 2018).

Garcia, Feltrin & Garda-Buffon (2018) also reported that the peroxidase enzyme has the ability to degrade zearalenone concentrations. According to the study, fusion of multifunctional recombinant enzymes ZHDCP with genes of ZEN hydrolases and carboxypeptidases has the ability to detoxify zearalenone in 2 h at pH and temperature of 35 °C (Azam et al., 2019). Many studies show that enzymes can be able to degrade zearalenone as expressed Table 2 (Table 2).

CONCLUSIONS

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. Future study should pay particular attention to the effects of toxin levels close to those experienced by humans, the choice of animal models, and the application of pathogenic mechanisms that differ greatly from humans. The emergence of microbial and enzyme preparations is quickly approaching the point at which it can be industrialized. The promise of these techniques for lessening the effects of mycotoxins in food and feed still need more study.

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Competing Interests

The authors declare there are no competing interests.

Author Contributions

- Jiregna Gari conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.

- Rahma Abdella conceived and designed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft.

Data Availability

The following information was supplied regarding data availability:

This is a literature review.

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 DOI [10.3390/toxins13040286](https://doi.org/10.3390/toxins13040286).
- Ahn JY, Kim J, Cheong DH, Hong H, Jeong JY, Kim BG. 2022.** An *in vitro* study on the efficacy of mycotoxin sequestering agents for aflatoxin B1, deoxynivalenol, and zearalenone. *Animals* **12**(3):333 DOI [10.3390/ani12030333](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 DOI [10.1016/j.microc.2021.106197](https://doi.org/10.1016/j.microc.2021.106197).
- Azam MS, Yu D, Liu N, Wu A. 2019.** Degrading ochratoxin A and zearalenone mycotoxins using a multifunctional recombinant enzyme. *Toxins* **11**(5):301 DOI [10.3390/toxins11050301](https://doi.org/10.3390/toxins11050301).
- 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 DOI [10.1186/s13568-018-0723-z](https://doi.org/10.1186/s13568-018-0723-z).
- Bin YS, Zheng HC, Xu JY, Zhao XY, Shu WJ, Li XM, Song H, Ma YH. 2021.** New biotransformation mode of zearalenone identified in *Bacillus subtilis* Y816 revealing a novel ZEN conjugate. *Journal of Agricultural and Food Chemistry* **69**:7409–7419 DOI [10.1021/acs.jafc.1c01817](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 DOI [10.3390/agronomy12040916](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* **12**:1–14 DOI [10.3390/toxins12020117](https://doi.org/10.3390/toxins12020117).
- Chen SW, Hsu JT, Chou YA, Wang HT. 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 DOI [10.1002/jsfa.8904](https://doi.org/10.1002/jsfa.8904).
- 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 DOI [10.1016/j.pep.2021.105933](https://doi.org/10.1016/j.pep.2021.105933).

- 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 DOI [10.3969/j.issn.1674-7968.2010.02.004](https://doi.org/10.3969/j.issn.1674-7968.2010.02.004).
- Cho KJ, Kang JS, Cho WT, Lee CH, Ha JK, Song KB. 2010.** *In vitro* degradation of zearalenone by *Bacillus subtilis*. *Biotechnology Letters* **32**(12):1921–1924 DOI [10.1007/s10529-010-0373-y](https://doi.org/10.1007/s10529-010-0373-y).
- Deng T, Yuan QS, Zhou T, Guo LP, Jiang WK, Zhou SH, Yang CG, Kang CZ. 2021.** Screening of zearalenone-degrading bacteria and analysis of degradation conditions. *China Journal of Chinese Materia Medica* **46**(20):5240–5246 DOI [10.19540/j.cnki.cjcmm.20210716.101](https://doi.org/10.19540/j.cnki.cjcmm.20210716.101).
- Eskola M, Kos G, Elliott CT, Hajšlová J, Mayar S, Krska R. 2020.** Worldwide contamination of food-crops with mycotoxins: Validity of the widely cited ‘FAO estimate’ of 25%. *Critical Reviews in Food Science and Nutrition* **60**(16):2773–2789 DOI [10.1080/10408398.2019.1612320](https://doi.org/10.1080/10408398.2019.1612320).
- 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 DOI [10.3389/fmicb.2020.00389](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 DOI [10.3390/toxins8100300](https://doi.org/10.3390/toxins8100300).
- Gajęcka M, Majewski MS, Zielonka Ł, Grzegorzewski W, Onyszek E, Lisieska-Zołnierczyk S. 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 DOI [10.3390/toxins13060396](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 DOI [10.1016/j.toxlet.2021.12.017](https://doi.org/10.1016/j.toxlet.2021.12.017).
- Garcia SO, Feltrin AP, Garda-Buffon J. 2018.** Zearalenone reduction by commercial peroxidase enzyme and peroxidases from soybean bran and rice bran. *Food Additives & Contaminants* **35**(9):1819–1831 DOI [10.1080/19440049.2018.1486044](https://doi.org/10.1080/19440049.2018.1486044).
- Greeff-Laubscher MR, Beukes I, Marais GJ, 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 DOI [10.1080/21501203.2019.1604575](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 DOI [10.3390/toxins13010046](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 DOI [10.1016/j.foodchem.2020.126877](https://doi.org/10.1016/j.foodchem.2020.126877).

- Harkai P, Szabó I, Cserhádi 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 DOI [10.1016/j.ibiod.2015.12.007](https://doi.org/10.1016/j.ibiod.2015.12.007).
- Harcárová M, Čonková E, Nad'P, Proškovcová M. 2022. Zearalenone Biodegradation by the Spp. and Spp. *Folia Veterinaria* **66**(1):70–74 DOI [10.2478/fv-2022-0008](https://doi.org/10.2478/fv-2022-0008).
- Hathout AS, Aly SE. 2014. Biological detoxification of mycotoxins: a review. *Annal Microbiology* **64**(3):905–919 DOI [10.1007/s13213-014-0899-7](https://doi.org/10.1007/s13213-014-0899-7).
- Hsu TC, Yi PJ, Lee TY, Liu JR. 2018. Probiotic characteristics and zearalenone-removal ability of a *Bacillus licheniformis* strain. *PLOS ONE* **13**(4):0194866 DOI [10.1371/journal.pone.0194866](https://doi.org/10.1371/journal.pone.0194866).
- Hui R, Hu X, Liu W, Zheng Y, Chen Y, Guo RT, Jin J, Chen CC. 2017. Characterization and crystal structure of a novel zearalenone hydrolase from *Cladophialophora bantiana*. *Acta Crystallographica Section F* **73**(9):515–519 DOI [10.1107/S2053230X17011840](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 DOI [10.3390/ani12151962](https://doi.org/10.3390/ani12151962).
- Ju J, Tinyiro SE, 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 DOI [10.1111/jfpp.14122](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 DOI [10.1016/j.lwt.2017.10.061](https://doi.org/10.1016/j.lwt.2017.10.061).
- Kabak B, Dobson AD, Var IL. 2006. Strategies to prevent mycotoxin contamination of food and animal feed: a review. *Critical Review Food Science and Nutrition* **46**(8):593–619 DOI [10.1080/10408390500436185](https://doi.org/10.1080/10408390500436185).
- Keller L, Abrunhosa L, Keller K, Rosa CA, 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 DOI [10.3390/toxins7083297](https://doi.org/10.3390/toxins7083297).
- 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 DOI [10.3390/toxins11100552](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 DOI [10.3390/ijms23031064](https://doi.org/10.3390/ijms23031064).
- Loi M, Fanelli F, Liuzzi VC, Logrieco AF, Mulè G. 2017. Mycotoxin biotransformation by native and commercial enzymes: present and future perspectives. *Toxins* **9**(4):111 DOI [10.3390/toxins9040111](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 Food Science and Technology* **96**:127–134 DOI [10.1016/j.tifs.2019.12.012](https://doi.org/10.1016/j.tifs.2019.12.012).
- Møller CO, Freire L, Rosim RE, Margalho LP, Balthazar CF, Franco LT, Sant’Ana AD, Corassin CH, Rattray FP, Oliveira CA. 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**:655386 DOI [10.3389/fmicb.2021.655386](https://doi.org/10.3389/fmicb.2021.655386).
- Mukherjee D, Royce SG, Alexander JA, Buckley B, Isukapalli SS, Bandera EV, Zarbl H, Georgopoulos PG. 2014. Physiologically-based toxicokinetic modeling of zearalenone and its metabolites: application to the Jersey girl study. *PLOS ONE* **9**(12):e113632 DOI [10.1371/journal.pone.0113632](https://doi.org/10.1371/journal.pone.0113632).
- Nahle S, Khoury AEI, 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 DOI [10.1186/s40550-022-00089-2](https://doi.org/10.1186/s40550-022-00089-2).
- Navale VD, Vamkudoth K. 2022. Toxicity and preventive approaches of Fusarium derived mycotoxins using lactic acid bacteria: state of the art. *Biotechnology Letters* **44**(10):1–16 DOI [10.1007/s10529-022-03293-4](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 DOI [10.1016/j.foodcont.2021.108429](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 dye-decolorizing peroxidase from *Streptomyces thermocarboxydus* combining catalytic properties of manganese peroxidase and laccase. *Toxins* **13**(9):602 DOI [10.3390/toxins13090602](https://doi.org/10.3390/toxins13090602).
- Ragoubi C, Quintieri L, Greco D, Mehrez A, Maatouk I, D’Ascanio V. 2021. Mycotoxin removal by *Lactobacillus* spp. and their application in animal liquid feed. *Toxins* **13**(3):185 DOI [10.3390/toxins13030185](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 DOI [10.1016/j.toxicon.2019.03.004](https://doi.org/10.1016/j.toxicon.2019.03.004).
- Ropejko K, Twaruzek M. 2021. Zearalenone and its metabolites-general overview, occurrence, and toxicity. *Toxins* **13**(1):35 DOI [10.3390/toxins13010035](https://doi.org/10.3390/toxins13010035).
- Singh K, Kumari A. 2022. Traditional mycotoxins and their health implications. *Mycotoxins and Mycotoxicoses* 27–64 DOI [10.1007/978-981-19-2370-8_3](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 DOI [10.1016/j.toxicon.2021.08.003](https://doi.org/10.1016/j.toxicon.2021.08.003).
- Średnicka P, Juszczyk-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 DOI [10.1016/j.fct.2021.112306](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 DOI [10.1093/bbb/zbab204](https://doi.org/10.1093/bbb/zbab204).
- Tang Y, Xiao J, Chen Y, Yu Y, Xiao X, Yu Y. 2013.** Secretory expression and characterization of a novel peroxiredoxin for zearalenone detoxification in *Saccharomyces cerevisiae*. *Microbiology Research* **168**:6–11 DOI [10.1016/j.micres.2012.08.002](https://doi.org/10.1016/j.micres.2012.08.002).
- Vega MF, Dieguez SN, Riccio B, Aranguren S, Giordano A, Denzoin L. 2017.** Zearalenone adsorption capacity of lactic acid bacteria isolated from pigs. *Brazilian Journal of Microbiology* **48**:715–723 DOI [10.1016/j.bjm.2017.05.001](https://doi.org/10.1016/j.bjm.2017.05.001).
- Wang N, Wu W, Pan J, Long M. 2019.** Detoxification strategies for zearalenone using microorganisms: a review. *Microorganisms* **7**(7):208 DOI [10.3390/microorganisms7070208](https://doi.org/10.3390/microorganisms7070208).
- Wang J, Xie Y. 2020.** Review on microbial degradation of zearalenone and aflatoxins. *GOST* **3**(3):117–125 DOI [10.1016/j.gaost.2020.05.002](https://doi.org/10.1016/j.gaost.2020.05.002).
- Wang JQ, Yang F, Yang PL, Liu J, Lv ZH. 2018.** Microbial reduction of zearalenone by a new isolated *Lysinibacillus* sp. ZJ-2016-1. *World Mycotoxin Journal* **11**(4):571–578 DOI [10.3920/WMJ2017.2264](https://doi.org/10.3920/WMJ2017.2264).
- 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 DOI [10.1016/j.foodcont.2017.01.021](https://doi.org/10.1016/j.foodcont.2017.01.021).
- 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 DOI [10.1016/j.cjche.2020.11.011](https://doi.org/10.1016/j.cjche.2020.11.011).
- Xia Y, Wu Z, He R, Gao Y, Qiu Y, Cheng Q. 2021.** Simultaneous degradation of two mycotoxins enabled by a fusion enzyme in food-grade recombinant *Kluyveromyces lactis*. *Bioresources Bioprocess* **8**:1–11 DOI [10.1186/s40643-021-00395-1](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*. *Microbiology Research* **193**:48–56 DOI [10.1016/j.micres.2016.09.004](https://doi.org/10.1016/j.micres.2016.09.004).
- Xu H, Wang L, Sun J, Wang L, Guo H, Ye Y. 2022.** Microbial detoxification of mycotoxins in food and feed. *Critical Review Food Science and Nutrition* **62**(18):4951–4969 DOI [10.1080/10408398.2021.1879730](https://doi.org/10.1080/10408398.2021.1879730).
- Xu J, Wang H, Zhu Z, Ji F, Yin X, Hong Q. 2016.** Isolation and characterization of *Bacillus amyloliquefaciens* ZDS-1: exploring the degradation of Zearalenone by *Bacillus* spp. *Food Control* **68**:244–250 DOI [10.1016/j.foodcont.2016.03.030](https://doi.org/10.1016/j.foodcont.2016.03.030).
- Yadav R, Yadav P, Singh G, Kumar S, Dutt R, Pandey AK. 2021.** Non-infectious causes of abortion in livestock animals-A. *International Journal of Livestock Research* **11**(2):1–13 DOI [10.5455/ijlr.20201031015650](https://doi.org/10.5455/ijlr.20201031015650).
- Yang WC, Hsu TC, Cheng KC, Liu JR. 2017.** Expression of the *Clonostachys rosea* lactonohydrolase gene by *Lactobacillus reuteri* to increase its zearalenone-removing ability. *Microbial Cell Factories* **16**(1):1–11 DOI [10.1186/s12934-017-0687-8](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
[DOI 10.1201/9781003248316-16](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. *Microbiology Research* **167(3)**:121–126
[DOI 10.1016/j.micres.2011.07.004](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
[DOI 10.1016/j.scitotenv.2019.135897](https://doi.org/10.1016/j.scitotenv.2019.135897).
- Zhu Y, Drouin P, Lepp D, Li XZ, Zhu H, Castex M, Zhou T. 2021.** A novel microbial zearalenone transformation through phosphorylation. *Toxins* **13(5)**:294
[DOI 10.3390/toxins13050294](https://doi.org/10.3390/toxins13050294).