
بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

THE 9TH NATIONAL FUNGUS DAY OF EGYPT
"FUNGI THROUGH THE LENS OF ONE HEALTH"
الفطريات من خلال عدسة صحة واحدة

MYCOTOXINS: HARM & BENEFIT

PROF. EMAN KHALIFA (EGYPT)

PROFESSOR OF MICROBIOLOGY & ACTING DEAN OF FACULTY OF VETERINARY MEDICINE – MATROUH UNIVERSITY

Overall thoughts about mycotoxins

- Natural toxins are the main causes of contamination of agricultural commodities and foodstuffs, according to the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) (FAO, 2022).
- These substances are poisonous secondary metabolites that are naturally produced by plants, bacteria, fungus, and algae as a defense against insects, enemies, and microbes (FAO, 2022).
- Food manufacturers and other companies suffer financial losses as a result of toxins, which can also cause major health issues like allergic responses, severe stomachaches, diarrhea, and even death (FAO, 2022).

Overall thoughts about mycotoxins

- Approximately 400 different kinds of mycotoxins, which are secondary metabolites made by fungus, are known to exist in nature and can contaminate unprocessed food and agricultural products (Marins-Gonçalves et al., 2023).

- Aflatoxins (AF), citrines (CIT), fumonisins (FM), ochratoxins (OT), patulins (PAT), trichothecenes (TCT), and zearalenone (ZEN) are the most common mycotoxin classes identified in environmental materials. These mycotoxin classes are very harmful to both people and animals (Marins-Gonçalves et al., 2023).

Overall thoughts about mycotoxins

- As a result, it necessitates the strict identification and measurement of raw agricultural commodities like barley, beans, corn, fruits, nuts, oats, peanuts, rice, soybeans, sugar beets, sugar cane, vegetables, and wheat, as well as the detection of these products in food items through the use of chemical or biological analysis (Marins-Gonçalves et al., 2023).

- The proliferation of fungus and the formation of mycotoxins in food products pose a risk to the environment and public health (Manning and Abbas, 2012).

Overall thoughts about mycotoxins

- Of the several mycotoxins; aflatoxin B1 (AFB1), deoxynivalenol (DON), and zearalenone (ZEN) are the most significant (Rodrigues and Naehrer, 2011).

- Among the most harmful xenobiotic; AFB1 is a strong carcinogen that has mutagenic, genotoxic, and hepatocarcinogenic properties (Mohammadi et al., 2014).

Overall thoughts about mycotoxins

- *Fusarium* species are the primary producers of a class of mycotoxins known as trichothecenes, the most common trichothecene; deoxynivalenol (DON), is one of the main mycotoxins present in corn, wheat, and barley. (Casteel et al., 2010).

- Deoxynivalenol (DON) can lead to ribosomal stress response-induced protein synthesis inhibition, immunological dysregulation, food rejection, impaired weight gain, and disruption of regular cell cycles (Pestka, 2008).

Overall thoughts about mycotoxins

- ZEN has also lately been implicated in genotoxicity, being one of the most potent naturally occurring estrogenic pollutants that affect development (Pfohl-Leszkowicz et al., 1995).

- Few research on the combined toxic effects of many mycotoxins have been performed to at this point and they have discovered that most of the time, synergistic or additive toxicities might be caused (Sun et al., 2015).

Overall thoughts about mycotoxins

- Globally, agricultural commodities are increasingly contaminated by AFB1, DON, and/or ZEN at the same time, an emerging trend. According to a survey; mycotoxins (Afla, DON, ZEN, FUM, and OTA) were found in 78% of 3300 tested samples (corn, wheat, barley, rice, soybean meal, corn gluten meal, dried distillers grains, and silage) in 2010. The percentage of mycotoxins that occurred together was as high as 42% (Rodrigues and Naehrer, 2011).

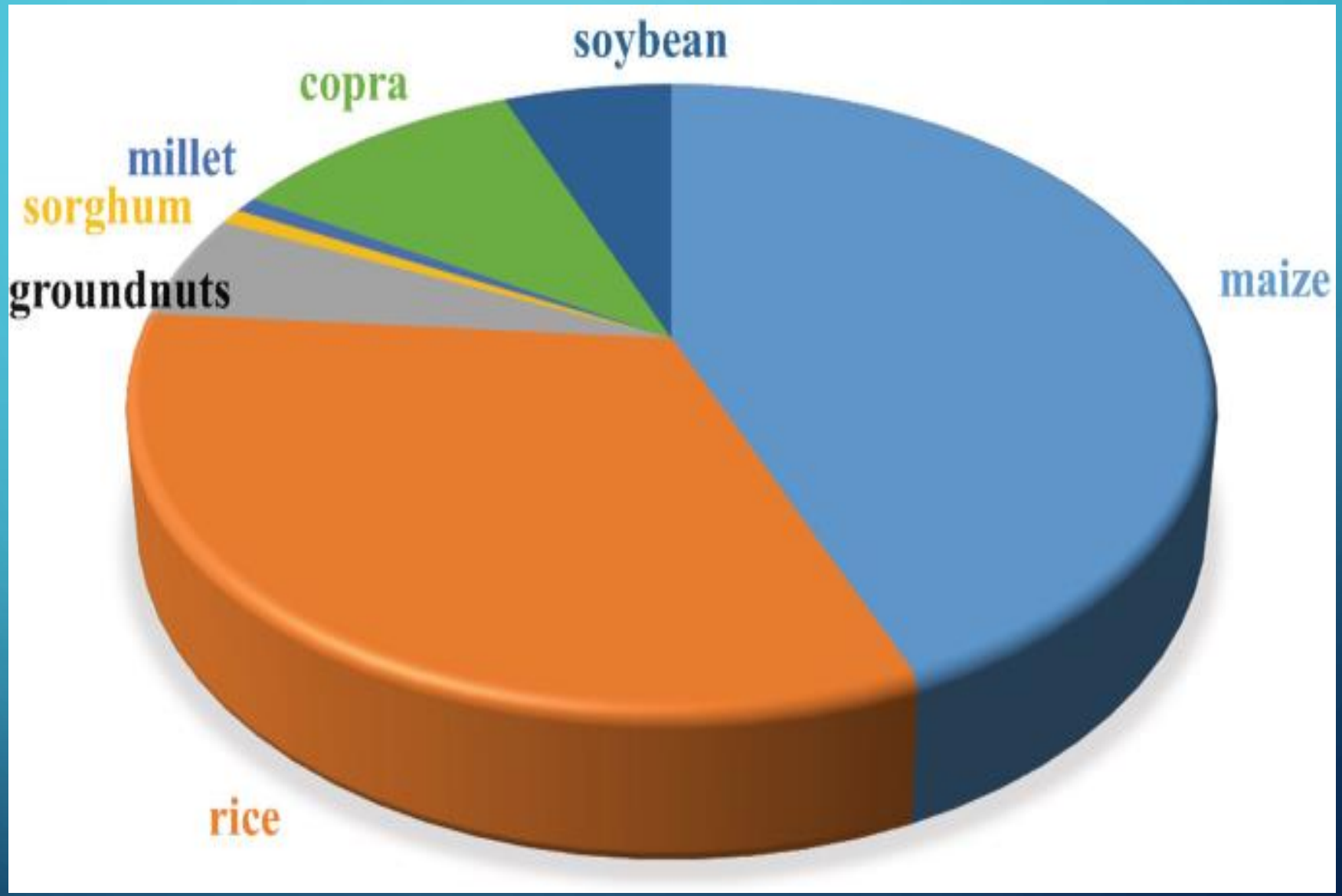
Overall thoughts about mycotoxins

- However, given that co-exposure to mycotoxins is a reality, a study recommended that risk assessment and acceptable exposure limit computations be done using the combined effect of these mycotoxins rather than their individual dose response (Zhoua et al., 2017).

Overall thoughts about mycotoxins

- Mycotoxins can be transferred from plants to humans by the eating of contaminated plant-based meals. They can also be found in animal products like meat and eggs.(Bonel, et al. 2011).

- Human also can be infected by coming into contact with poisonous dust and air (Niculita-Hirzel et al., 2016)


soybean
copra
millet
sorghum
groundnuts
maize
rice

Overall thoughts about mycotoxins

- Exposure to these toxins is more likely to be widespread in regions of the world with inadequate pest infestation control measures for crops, roads, and storage facilities; on the other hand, it can also be widespread in highly poor societies where people consume only what is readily available rather than what is desirable. (Zinedine et al., 2009).

- Continuous exposure to mycotoxins is also typical in areas without laws or regulations protecting the public's food intake. (Zinedine et al., 2009).

Overall thoughts about mycotoxins

- In developed nations, there exists a possibility of mycotoxin exposure, particularly in populations where inadequate food handling practices are prevalent. This increases the population's susceptibility to diseases caused by mycotoxin (Zinedine et al., 2009).

- Mycotoxins pose a risk to human health since they have the potential to cause serious, permanent harm to people's health, including cancer, especially in underdeveloped countries. Since most mycotoxins are resistant to heat within the typical range of cooking temperatures, it is known that there is very little that can be done to remove them from food and feed once they have become infected. **(Omotayo et al., 2019)**

Mycotoxins' occurrence

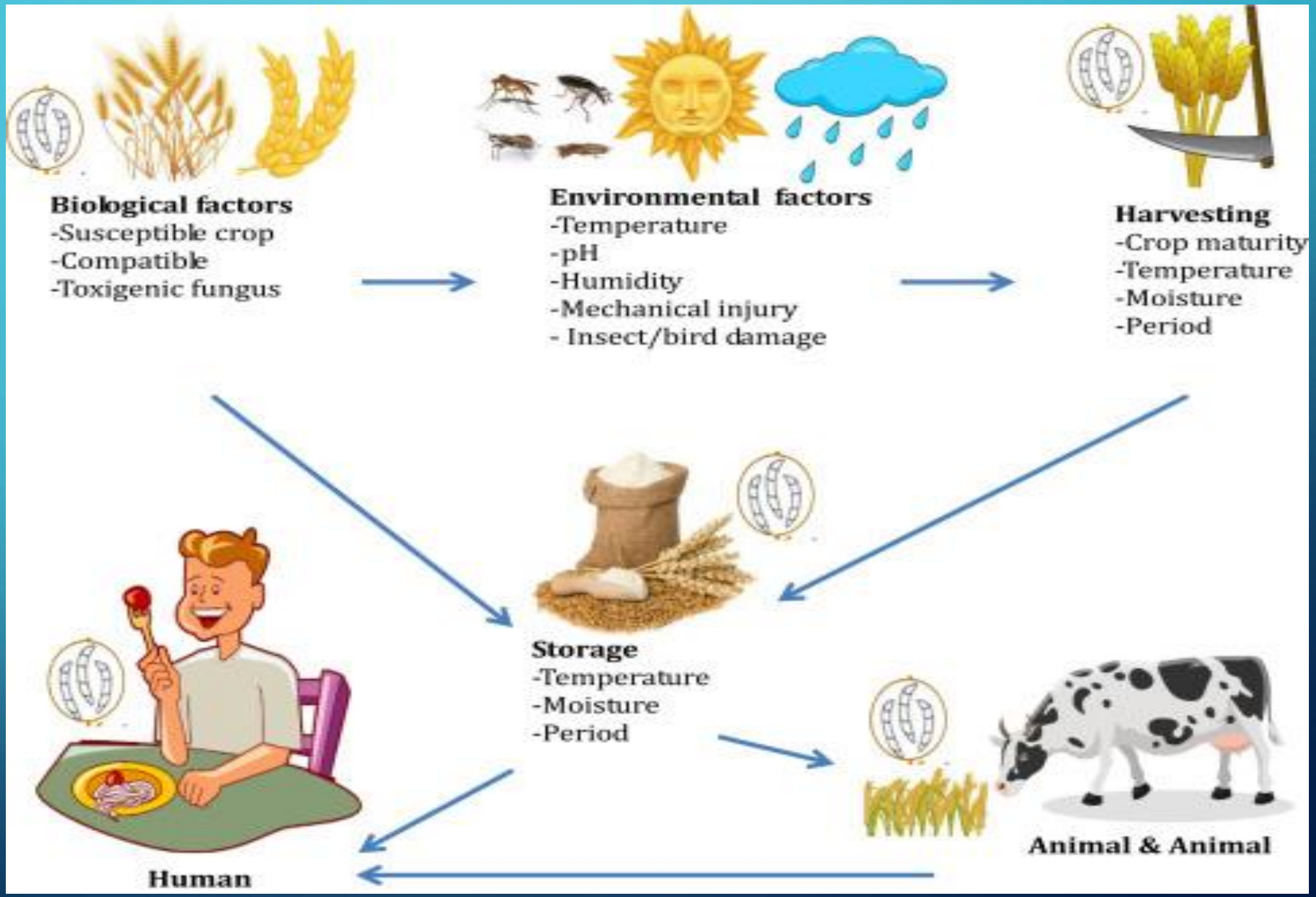
- Certain fungal species, including *Alternaria*, *Aspergillus*, *Claviceps*, *Fusarium*, and *Penicillium*, have been found in raw agricultural products associated with susceptible crops (Marins-Gonçalves et al., 2023).

- Other factors that may contribute to this fungal presence include high temperatures, high moisture content, inadequate pre- and post-harvest practices, and a lack of proper care and hygiene during the handling and storage processes, permits the synthesis of diverse mycotoxin kinds and concentrations. (Marins-Gonçalves et al., 2023).

Mycotoxins' occurrence

- Mycotoxins can also spoil dairy products, meat, and their byproducts. Furthermore, because the majority of mycotoxins are chemically stable, they can persist in cooked foods and contaminate industrialized goods while being stored, processed, and consumed (Marins-Gonçalves et al., 2023).

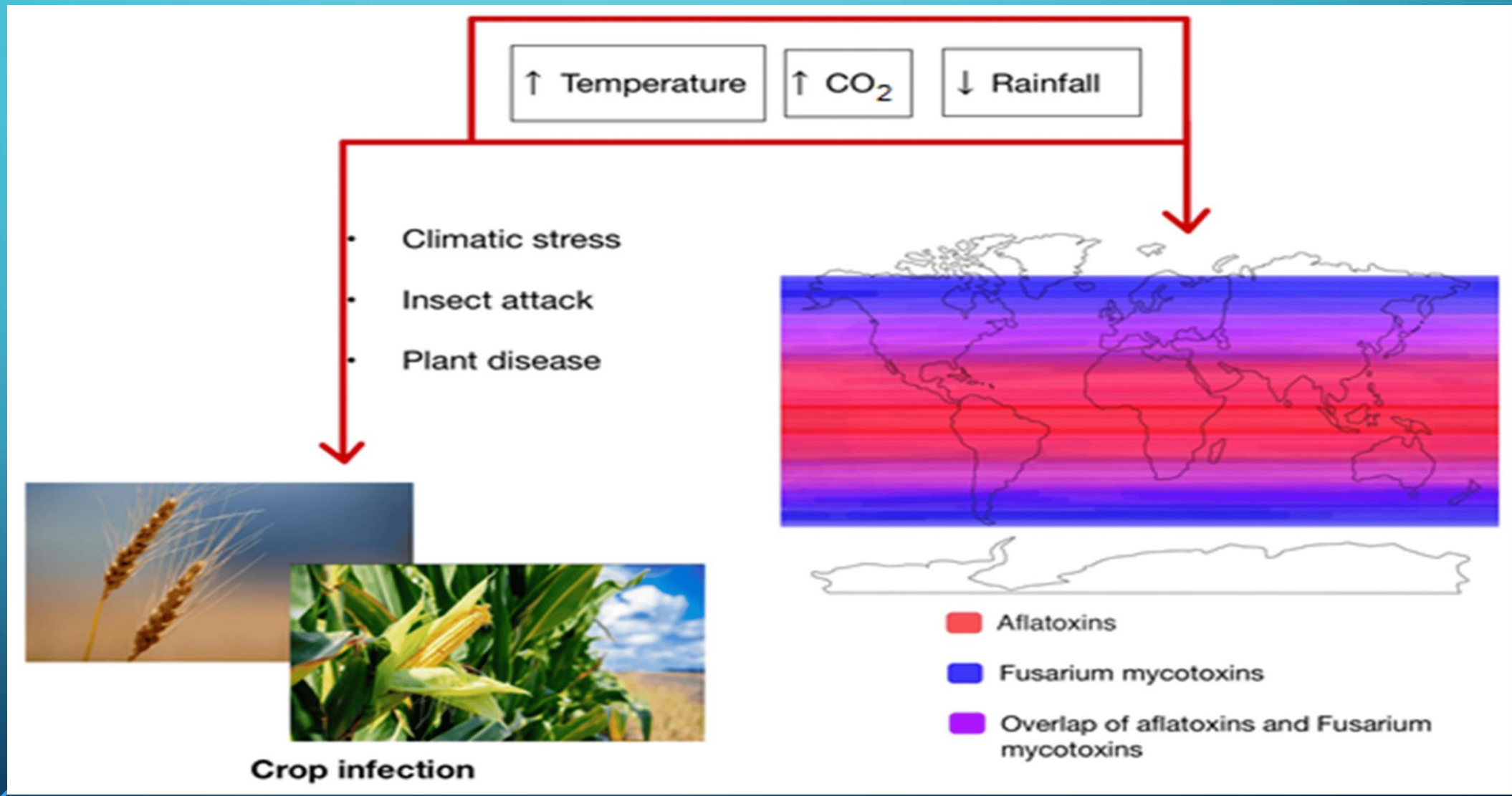
- It has recently been revealed that mycotoxins can be found in drinking water, wastewater, and soil (Juraschek et al., 2022)


Biological factors
-Susceptible crop
-Compatible
-Toxigenic fungus
Environmental factors
-Temperature
-pH
-Humidity
-Mechanical injury
- Insect/bird damage
Harvesting
-Crop maturity
-Temperature
-Moisture
-Period
Storage
-Temperature
-Moisture
-Period
Human
Animal & Animal

Mycotoxins' occurrence

- In addition, the presence of mycotoxins in fruit products, cereal-based infant formula, and breast milk was investigated because these items expose consumers to a combination of mycotoxins at the same time, which may have synergistic effects under circumstances where mycotoxins are hazardous (Coppa et al., 2019).

Mycotoxins' occurrence with relation to climate changes



Mycotoxins' occurrence with relation to climate changes

Mycotoxins' types

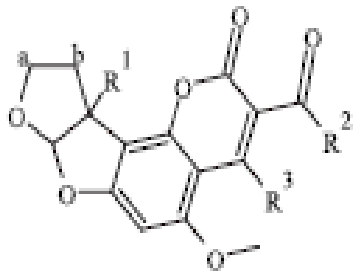
- The primary categories of mycotoxins that are linked to contaminations of food and agricultural products are free mycotoxins such ochratoxins (OT), fumonisins (FM), aflatoxins (AF), citrines (CIT), patulins (PAT), trichothecenes (TCT), and zearalenone (ZEN) (Tan, et al., 2023).

- But recently, modified mycotoxins have also been mentioned as possible pollutants (Tan, et al., 2023).

Mycotoxins' types

- Mycotoxins that have undergone modification can have altered structures, polarities, solubilities, and levels of toxicity. They can also coexist with free mycotoxin and exceed the amount found in food items. These metabolites are created during the processing of contaminated raw agricultural commodities or are transformed to the parent toxin during animal and human metabolism (Tan, et al., 2023).

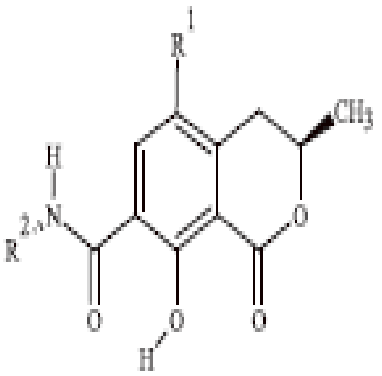
The primary mycotoxin chemical structures, both free and modified, the crops (raw and processed) that contain them, their hazardous effects on humans, and the official WHO analysis method are all included in the following tables

Mycotoxin free	Mycotoxin modified		Agricultural commodities where can be found	Toxic effects in human	Official Method of analysis
Aflatoxin (AF) 	AFB1	R1 H R2-R3 link -CH_2-CH_2- a-b bond C=C	Maize, pearl millet, rice, sorghum, wheat, black pepper, chilies, coriander, ginger, turmeric, oilseeds, almond, pistachio, walnut, coconut, milk (animal and human) and butter	Highly toxic, mutagenic, teratogenic, and carcinogenic	HPLC
	AFB2	R1 H R2-R3 link -CH2-CH2- a-b bond C-C			
	AFG1	R1 H R2-R3 link -O-CH2-CH2- a-b bond C=C			
	AFG2	R1 H R2-R3 link -O-CH2-CH2- a-b bond C-C			
	AFM1	R1 OH R2-R3 link -CH2-CH2- a-b bond C=C			

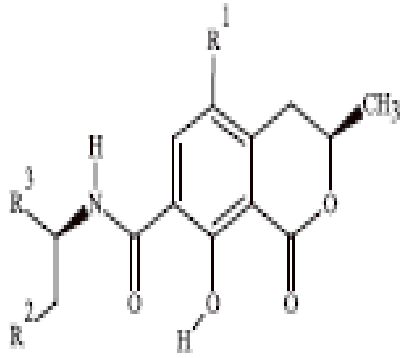
Aflatoxins: AF are secondary metabolites of *Aspergillus* fungi

(Bhat, et al., 2010)

Ochratoxin (OT)



OTA and OTB

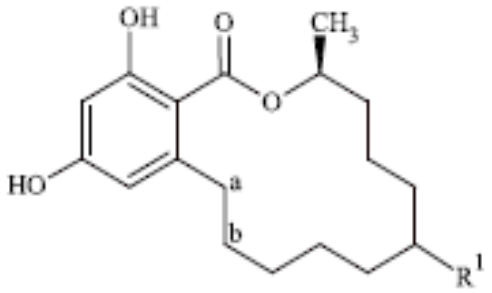


OTC

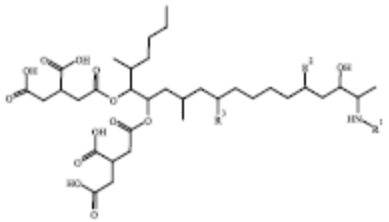
OTA	R1	Cl	Beer, cereals, coffee, cocoa, dried fruits, grapes, spices, wine, dairy and meat products	Embryotoxicity, genotoxicity, hepatotoxicity, immunotoxicity, mutagenicity, nephrotoxicity and teratogenicity	HPLC
	R2	C(COOH)CH2(C6H5)			
OTB	R1	H			
	R2	C(COOH)CH2(C6H5)			
OTC	R1	Cl			
	R2	(C6H5)			
	R3	COOCH2CH3			

Ochratoxins: The fungus *Aspergillus* and *Penicillium* are the source of OT (Wang et al., 2022)

Zearalenona (ZEN)



ZEN	R1	=O	Maize and several other grains crops plants, barley, grape rice, millet, oat, peanut, rye, wheat and grain products such as chips, flask and tortillas	High affinity for estrogen receptors, causing reproductive and fertility difficulties in mammals
	a-b bond	-C=C-		
α-ZEL	R1			
	a-b bond	-C=C-		
β-ZEL	R1			
	a-b	-C=C-		
FMB1	R1	H	Maize, grains crops plants, barley, grape rice, millet, oat, peanut, rye, wheat and grain products such as chips, flask and tortillas	Esophageal cancer, malformation of the neural tube, nerve damage, anencephaly and stillbirth
	R^2	OH		
	R^3	OH		
FMB2	R^1	H		
	R^2	OH		
	R^3	H		
FMB3	R^1	H		
	R^2	H		
	R^3	OH		
	bond			
β-ZAL	R1			
	a-b bond	-C-C-		

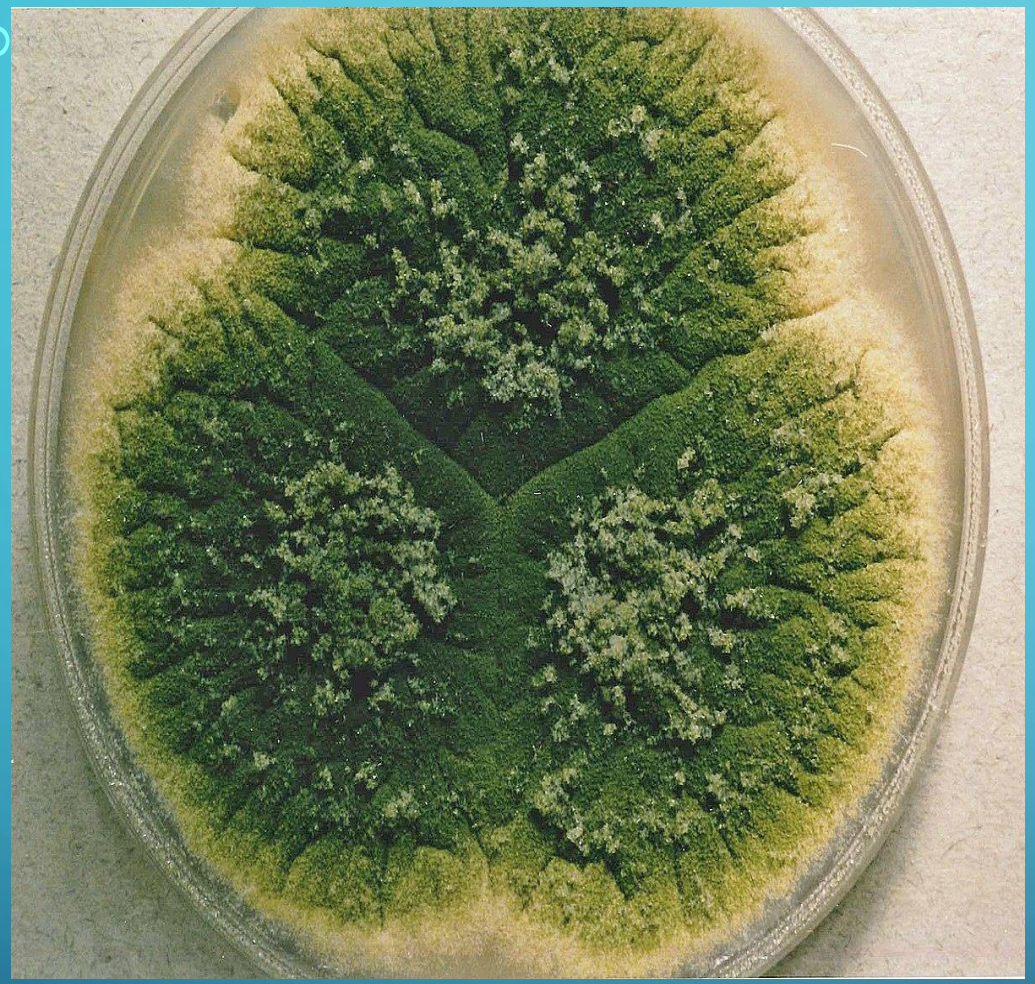


Zearalenone: ZEN secreted from the fungus *Fusarium*

Fumonisins: FM are secondary metabolites found in cereals that are produced by the pathogenic fungus *Fusarium* and *Aspergillus* (Ocampo-Acu˜na et al., 2023)

Fish and mycotoxins

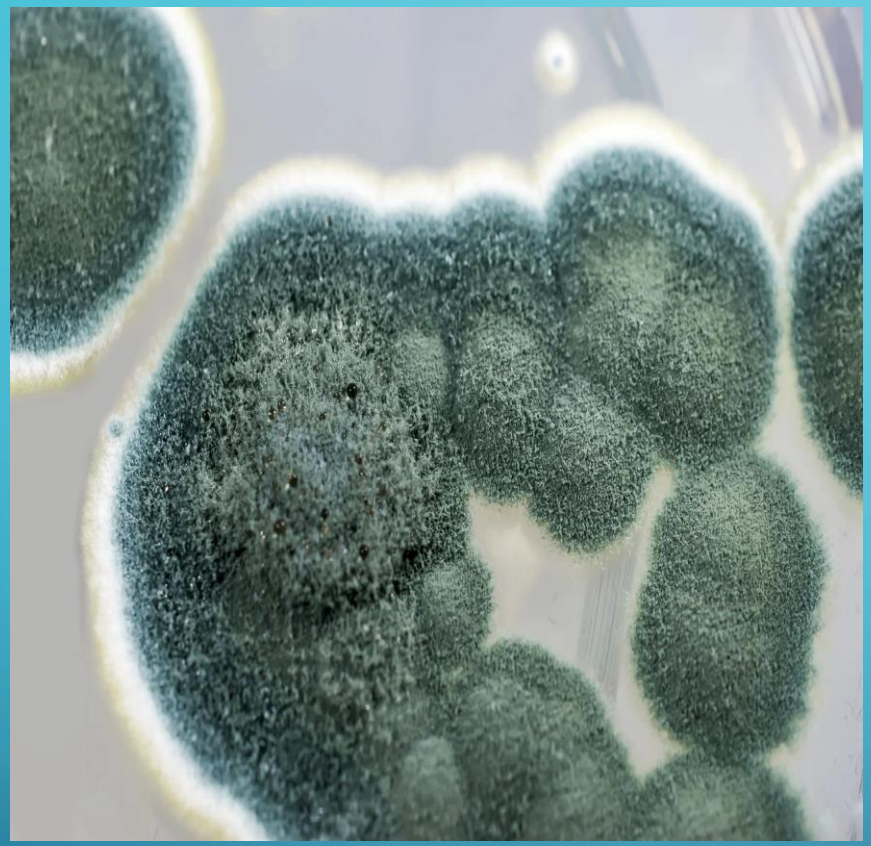
- Farm-raised fish are susceptible to mycotoxin exposure from feed and runoff from grain fields that drain into water stream (Schenzel et al., 2012)
- The mycotoxins are considered aquatic system micropollutants because the amounts of them in drainage and river water are similar to those of pesticides (Bucheli et al., 2008).
- Apart from the mycotoxins present in drainage water that could endanger fish health; the mycotoxins in aquafeed can also have a significant impact on fisheries. (Pietsch et al., 2013).
- As well as plant materials are increasingly being used in aquafeed formulations for fish breeding, which raises the risk of aflatoxin contamination (Santacroce et al., 2008).

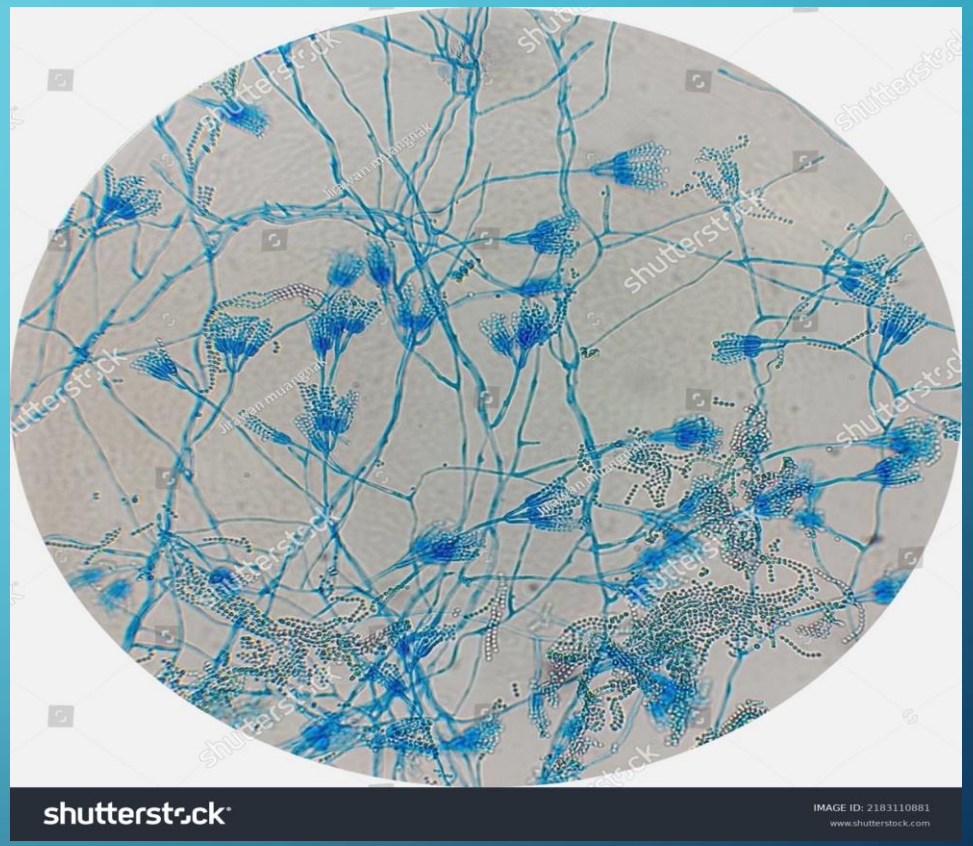


Aspergillus parasiticus

Aspergillus flavus

Fusarium spp





Penicillium spp

Benefits of Mycotoxins

- Trichothecene mycotoxins has antiviral effect as inhibiting the replication of Herpes simplex virus (Tani et al., 1995).
- Penicillin secreted by *Penicillium* can be used as antibiotic for treatment of several bacterial diseases.
- Immunosuppressants (*Cyclosporine*).
- Control of postpartum hemorrhage and migraine headaches (ergot alkaloids secreted by *Claviceps purpurea*)

Recommendations

- The evaluation of the risks that humans face from eating contaminated food led to the creation of particular laws that analyze the types, concentrations, and presence of mycotoxins in food and agricultural products.

- Therefore, it is necessary to establish appropriate analytical processes for the identification and quantification of mycotoxins in the free or modified form, in low concentration, and in complicated samples in order to assure that they meet legislation, food safety, and consumer health.

Recommendations

- It is critical that producers of agricultural commodities develop more environmentally friendly, quick, and accurate mycotoxin extraction techniques.
- More investigation is required into the molecular process of mycotoxins production, particularly with regard to the new mycotoxins.
- Understanding the chemotypes of mycotoxins may help control fungal infections and promote resistance in grain production, resulting in higher-quality grain.

Recommendations

- More studies will also advance our knowledge of the ecology and epidemiology of mycotoxins members, which could be useful in developing models to estimate the probability of epidemics and the generation of mycotoxin.
- It is advised that more research be done on the toxicity of mycotoxins in fish since fish seem to be very susceptible to them.

Recommendations

- Encouraging proper prevention and control of these dangerous chemicals in agricultural products while they are still in the field is important because it will significantly slow the spread of mycotoxins and, in turn, the number of illnesses caused by mycotoxin.


Inactivate, destroy or remove the toxin
TOXINS
NON TOXIC
NON TOXIC
NON TOXIC
Not leave or produce toxic residues
Not change the nutritional, organoleptical, or technological properties of food
Mycotoxins
Destroy fungal spores, preventing the production of mycotoxins
Environmentally friendly
Cost Effective

References

- Manning, B.B., Abbas, H.K., 2012. The effect of Fusarium mycotoxins Deoxynivalenol, Fumonisin, and Moniliformin from contaminated moldy grains on aquaculture fish. Toxin Rev. 31, 11–15.
- Schenzel, J., Forrer, H.-R., Vogelgsang, S., Hungerbuehler, K., Bucheli, T.D., 2012. Mycotoxins in the environment: i. Production and emission from an agricultural test field. Environ. Sci. Technol. 46, 13067–13075.
- Bucheli, T.D., Wettstein, F.E., Hartmann, N., Erbs, M., Vogelgsang, S., Forrer, H.-R.,Schwarzenbach, R.P., 2008. Fusarium mycotoxins: overlooked aquatic micropollutants? J. Agric. Food Chem. 56, 1029–1034.
- Santacroce, M.P., Conversano, M., Casalino, E., Lai, O., Zizzadoro, C., Centoducati, G., Crescenzo, G., 2008. Aflatoxins in aquatic species: metabolism, toxicity and perspectives. Rev. Fish Biol. Fish. 18, 99–130.
- Richard, J.L., 2007. Some major mycotoxins and their mycotoxicoses—An overview. Int. J. Food Microbiol. 119, 3–10.
- Mohammadi, A., Mehrzad, J., Mahmoudi, M., Schneider, M., 2014. Environmentally relevant level of Aflatoxin B1 dysregulates human dendritic cells through signaling on key toll-like receptors. Int. J. Toxicol. 33, 175–186.
- Casteel, M., Nielsen, C., Didier, A., Dietrich, R., Märtlbauer, E., 2010. Induction of MAPK-dependent transcription factors by Deoxynivalenol in human cell lines. Mycotoxin Res. 26, 9–14.

References

- Pestka, J.J., 2008. Mechanisms of Deoxynivalenol-induced gene expression and apoptosis. Food Addit. Contam. Part A-Chem. Anal. Control Exposure Risk Assess. 25, 1128–1140.
- Pfohl-Leszkowicz, A., Chekir-Ghedira, L., Bacha, H., 1995. Genotoxicity of Zearalenone, an estrogenic mycotoxin: DNA adduct formation in female mouse tissues. Carcinogenesis 16, 2315–2320.
- Sun, L.H., Lei, M.Y., Zhang, N.Y., Gao, X., Li, C., Krumm, C.S., Qi, D.S., 2015. Individual and combined cytotoxic effects of Aflatoxin B1, Zearalenone, Deoxynivalenol and Fumonisin B1 on BRL 3A rat liver cells. Toxicon 95, 6–12.
- Rodrigues, I., Naehrer, K., 2011. Biomin Survey 2010: mycotoxins inseparable from animal commodities and feed. All About Feed 2, 17–20.
- Zhoua, H., Georgec, S., Lid, C., Gurusamyb, S., Suna, X., Gongd, Z. and Qiana, H., 2017. Combined toxicity of prevalent mycotoxins studied in fish cell line and zebrafish larvae revealed that type of interactions is dose-dependent. Aquatic Toxicology 193 (2017) 60–71.
- Food and Agriculture Organization of the United Nations, FAO Publications Catalogue 2022, FAO Publ. Cat, 2022, https://doi.org/10.4060/CC2323EN, 2022.
- Marins-Gonçalves, L., Ferreira, M. M., Guidi, L. R., De Souza, D. 2023. Is chemical analysis suitable for detecting mycotoxins in agricultural commodities and foodstuffs? Talanta 265 (2023) 124782

References

- Juraschek, L. M., A. Kappenberg, W. Amelung, Mycotoxins in soil and environment, Sci. Total Environ. 814 (2022), https://doi.org/10.1016/j. scitotenv.2021.152425.
- Coppa, C. F., A. Mousavi Khaneghah, P. Alvito, R. Assunç˜ao, C. Martins, I. Es¸, B.L. Gonçalves, D. Valganon de Neeff, A.S. Sant'Ana, C. H. Corassin, C.A.F. Oliveira, The occurrence of mycotoxins in breast milk, fruit products and cereal-based infant formula: a review, Trends Food Sci. Technol. 92 (2019) 81–93, https://doi.org/10.1016/j.tifs.2019.08.014.
- Bhat, R., R.V. Rai, A.A. Karim, Mycotoxins in food and feed: present status and future concerns, Compr. Rev. Food Sci. Food Saf. 9 (2010) 57–81, https://doi. org/10.1111/J.1541-4337.2009.00094.X.
- Wang, L., X. Hua, J. Shi, N. Jing, T. Ji, B. Lv, L. Liu, Y. Chen, A. Ochratoxin, Occurrence and recent advances in detoxification, Toxicon 210 (2022) 11–18, https://doi.org/10.1016/j.toxicon.2022.02.010.
- Ocampo-Acu˜na, Y.D., E. Salazar-Rios, M. ´Angeles Ramírez-Cisneros, M. Yolanda Rios, Comprehensive review of liquid chromatography methods for fumonisin determination, a 2006-2022 update, Arab. J. Chem. (2023), 104716, https://doi. org/10.1016/J.ARABJC.2023.104716.
- Tani, N., Yoshiko Dohi, Yoshiki Onji, and Kunio Yonemasu. 1995. Antiviral Activity of Trichothecene Mycotoxins (Deoxynivalenol, Fusarenon-X, and Nivalenol) against Herpes Simplex Virus Types 1 and 2. Microbiol. Immunol., 39(8), 635-637.
- Bonel, L., Vidal, J.C., Duato, P. and Castillo, J.R. (2011) An electrochemical competitive biosensor for ochratoxin A based on a DNA biotinylated aptamer. Biosens. Bioelectron., 26, 3254- 3259.

References

- Niculita-Hirzel, H., Hantier, G., Storti, F., Plateel, G. and Roger, T. (2016) Frequent occupational exposure to Fusarium mycotoxins of workers in the swiss grain industry. Toxins, 8, 370.
- Zinedine, A. and Mañes, J. (2009) Occurrence and legislation of mycotoxins in food and feed from Morocco. Food Control, 20, 334-344.
- Omotayo, O. P., Abiodun Olusola Omotayo2, Mulunda Mwanza and Olubukola Oluranti Babalola. 2019. Prevalence of Mycotoxins and Their Consequences on Human Health. Toxicol. Res. Vol. 35, No. 1, pp. 1-7. https://doi.org/10.5487/TR.2019.35.1.001


Thank You