

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Introductory Chapter: *Fusarium* - Pathogenicity, Infections, Diseases, Mycotoxins and Management

Tulin Askun

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.76507>

1. Introduction

The genus *Fusarium* contains pathogens that can cause significant harm to humans, animals and plants by infecting vegetables, grains and seeds and causing diseases in humans and animals. *Fusarium oxysporum*, *F. solani* and *F. fujikuroi* complexes are of great importance worldwide especially as a plant, human and animal pathogen.

Identifying *Fusarium* species is not easy. Currently, scientists are focused on identifying *Fusarium* species using molecular techniques, such as genetic markers and polymerase chain reaction-restriction fragment length polymorphism, for analyzing the rDNA internal transcribed spacer region.

The aim of this book is to highlight the new information reported by numerous studies on *Fusarium* species. The primary aims of this book are the following:

- (a) To provide an overview of historical importance and taxonomy of *Fusarium* species
- (b) To understand the mechanism of *Fusarium* infections and the factors that cause the infections
- (c) To discuss *Fusarium* species-caused diseases, pathogen diversity and host range in plants
- (d) To discuss mycotoxin contaminations in cereals
- (e) To discuss plant secondary metabolites as well as anti-fungal and anti-mycotoxigenic compounds
- (f) To discuss plant-*Fusarium* interactions
- (g) To discuss the antagonistic activity of *Trichoderma* and *Fusarium* species

- h) To discuss genetic diversity, genetic resistance and molecular markers to investigate population diversity
- (i) To discuss the environmental conditions that enable the opportunistic growth of *Fusarium*
- (j) To discuss the distribution and evolution of the genes responsible for mycotoxin biosynthesis
- (k) To discuss the steps that can be taken to prevent toxin production
- (l) To discuss suitable approaches for *Fusarium* species disease management
- (m) To discuss development of *Fusarium*-resistant cultivars to reduce the diseases caused by *Fusarium* species on a wide scale

2. Plant pathogens and cereals

Fusarium attacks numerous plants and cereals that are important for human and animal nutrition. It specifically infects certain parts of them, such as grains, seedlings, heads, roots or stem, and causes various diseases, reduced commercial yield, and decrease in product quality [1]. *Fusarium* head blight (FHB) [2, 3], foot (FR) and root rot (RR) [4] and crown rot (CR) are among the major diseases caused by them. FHB produced by *F. graminearum* (teleomorph *Gibberella zeae*, Schwabe) causes starch and protein losses in cereals [5]. *Fusarium* species are saprophytic and are found commonly growing on the plants as a pathogen. *F. proliferatum* is a plant pathogen that is capable of infecting many important crops. *F. oxysporum* f.sp. *cubense* (FOC) causes *Fusarium* wilt, which is the most destructive disease of banana [6]. Many *Fusarium* species from the *F. solani* species complex (FSSC) are pathogenic and virulent. FSSC causes diseases in many agriculturally important crops, such as FR and/or RR of the infected host plant and causes necrosis. Symptoms, such as wilting, stunting and chlorosis, vary widely according to FSSC pathogenesis and the host plant species. Necrosis depends on the severity of fungal development [4]. Two of the most serious diseases of wheat known globally are *Fusarium* CR and *Fusarium* FHB.

Stephens et al. [7] investigated the CR disease in wheat infected by *F. graminearum* and reported that CR developed in three stages. In the first stage, the *F. graminearum* biomass significantly increased within 2 days after inoculation. At this stage, there was germination of spores and superficial hyphal growth on the leaf sheath. In the second stage, the fungal biomass significantly decreased over 2 weeks. At this stage, the fungus penetrated from the outer parts of the leaf sheath to the leaf sheath base. In the third stage, biomass of *F. graminearum* increased significantly, and this increase correlated with fungal colonization on wheat and showed that the fungal biomass was being formed as fungal colonization on wheat crown parenchyma.

3. *Fusarium* infections in humans

Fusarium species cause superficial, locally invasive and diffuse infections in humans. Although *Fusarium verticillioides*, including *F. moniliforme* and *F. fujikuroi* species complex [8],

are opportunistic pathogens, the species in the *F. solani* complex include pathogenic species [9]. *F. solani*, *F. oxysporum*, *F. verticillioides* and *F. proliferatum* infect the immune-compromised patients. Sidhu et al. [10] reported that prevalent meningospondylodiscitis in an elderly diabetic patient caused by *F. oxysporum*. *F. sacchari*, *F. anthophilum*, *F. chlamydosporum* and *F. dimerum* was also thought as related to human disease. Guendouze-Bouchefa et al. [11] reported a rare case of perinephric abscess in a child caused by *F. chlamydosporum*.

The members of *F. solani* and *F. oxysporum* species complexes are known to include the agents that cause human infections worldwide. *F. solani* can adhere to and damage the corneal membrane [12]. Some *Fusarium* species, such as *F. dimerum*, are associated with keratomycosis, particularly in the bad hygiene conditions.

4. *Fusarium* diseases in animals

Fusarium mycotoxins affect the growth, reproduction and hormonal condition of the animal. The effect of these mycotoxins on animals depends on the quantity of mycotoxin intake. After intake, these mycotoxins arrive at the gastrointestinal epithelial cell layer which is covered by the mucous secreted from goblet cells [13, 14].

Although deoxynivalenol (DON) and fumonisin-B1 (FB1) increase the permeability of intestinal epithelial cell layer in humans, animals and birds, they worsen the viability and proliferation of intestinal epithelial cells. High doses of mycotoxins may cause abdominal distress, diarrhea, cardiac insufficiency, emesis and even death in pigs and equine leukoencephalomalacia (ELEM) in horses [15]. Through *in vivo* and *in vitro* experimental studies, Cortinovis et al. [16] demonstrated that ZEN and its metabolites markedly up-regulated estrogen secretion in the reproductive organs.

ZEN is closely associated with infertility, decreased milk production and hyperestrogenism [17]. Cortinovis et al. [16] reported that ZEN directly affect ovarian cells and alter oocyte maturation under *in vitro* conditions; conversely, under *in vivo* conditions, this mycotoxin affected ovulation and puberty onset and caused morphological and functional disorders. T-2 toxin (T-2) causes cutaneous lesions in the mount and intestinal membrane and reduces egg production in poultry [18].

5. Mycotoxins and mycotoxin-producing conditions

Fusarium mycotoxins are very common worldwide. They exist in many plants and in various compositions. The major *Fusarium* mycotoxins are FB1, trichothecenes [e.g. DON, nivalenol (NIV), T-2 and ZEN] [19–21]. The most important species that is common in Europe is *F. graminearum*. In the past, *Fusarium* genus members were mostly not considered as pathogens in the field. However, *F. proliferatum* and *F. verticillioides* are of great importance as the main producers of the most dangerous *Fusarium* mycotoxins [22, 23]. Worldwide mycotoxin occurrence in maize and wheat/bran samples with their median and maximum levels were given in **Figure 1** [24, 25].

Shi et al. [5] evaluated the mycotoxins from 20 of the most common *Fusarium* species and sorted them into the following three groups based on their molecular characterization (**Figure 2**). Group-1 comprised fusaric acid producers and was further divided into two subgroups. Subgroup-I comprised *F. fujikuroi*, *F. solani*, *F. verticillioides* and *F. proliferatum* that produce fusaric acid and fumonisins; subgroup-II comprised *F. musae*, *F. equiseti*, *F. temperatum*, *F. subglutinans*, *F. tricinctum*, *F. oxysporum*, *F. concentricum*, *F. sacchari* and *F. andiyazi* that produce only fusaric acid. According to the classification of *Fusarium* mycotoxins, type-A trichothecene producers comprising *F. polyphialidicum*, *F. sporotrichioides* and *F. langsethiae* formed the Group-II, and type-B trichothecene producers comprising *F. meridionale*, *F. culmorum*, *F. graminearum* and *F. poae* formed Group-III.

In the presence of *Fusarium* species in plants, the contamination with fumonisins was shown in wheat [26], garlic [27], and asparagus [28]. The most affected plants, that is, maize, beans, soybean [29], rice [30], and sorghum [31] were specifically infected by *Gibberella fujikuroi* species complex (*F. proliferatum*, *F. verticillioides* and *F. andiyazi*) [29, 32].

Guidance values for *Fusarium* mycotoxins were set in Commission Recommendation 2006/576/EC [33]. Recommended values for the *Fusarium* mycotoxins DON, ZEA and fumonisins were set in "Commission Recommendation 2006/576/EC" [33]. For T-2 and HT-2 toxin, indicative

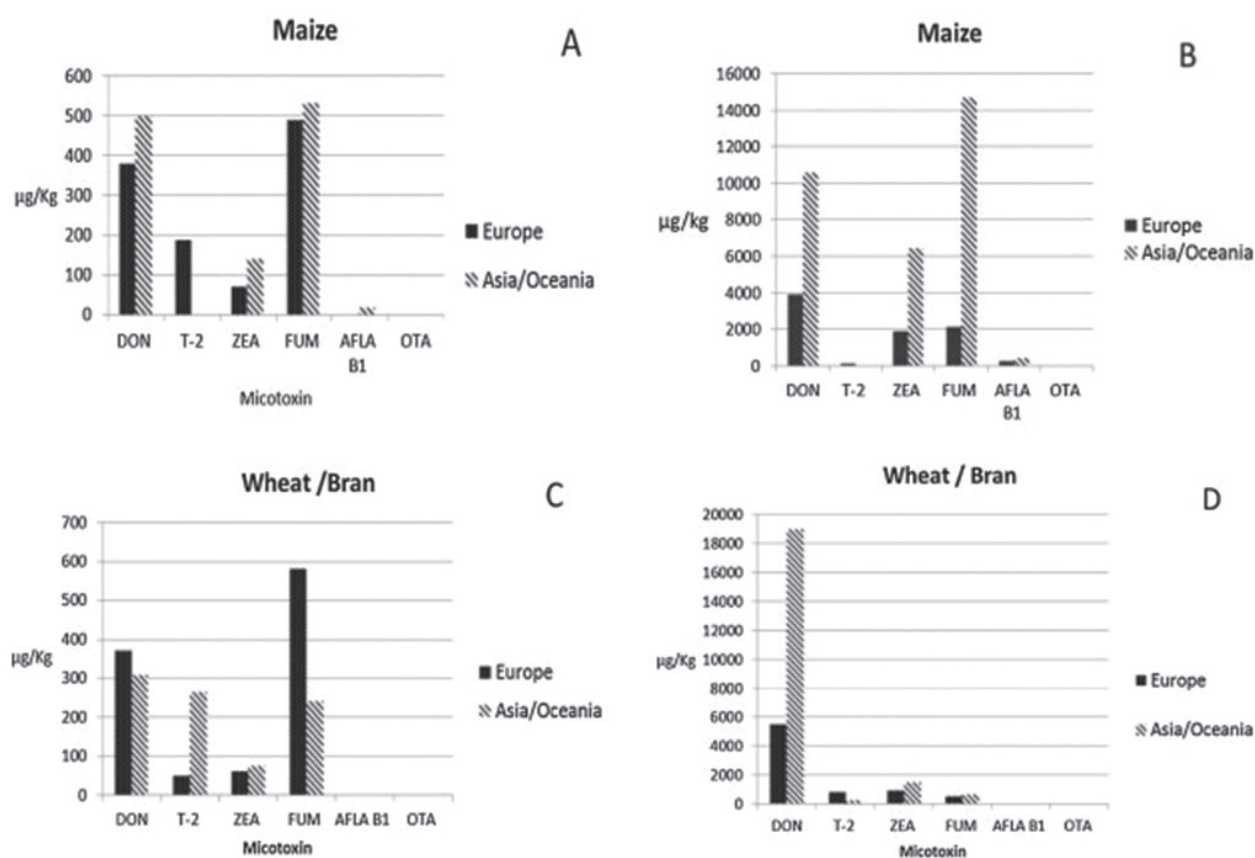


Figure 1. Worldwide mycotoxin occurrence (µg/kg) in maize and wheat/bran samples (A, C: Median of positive samples; B, D: Maximum levels) [24, 25].

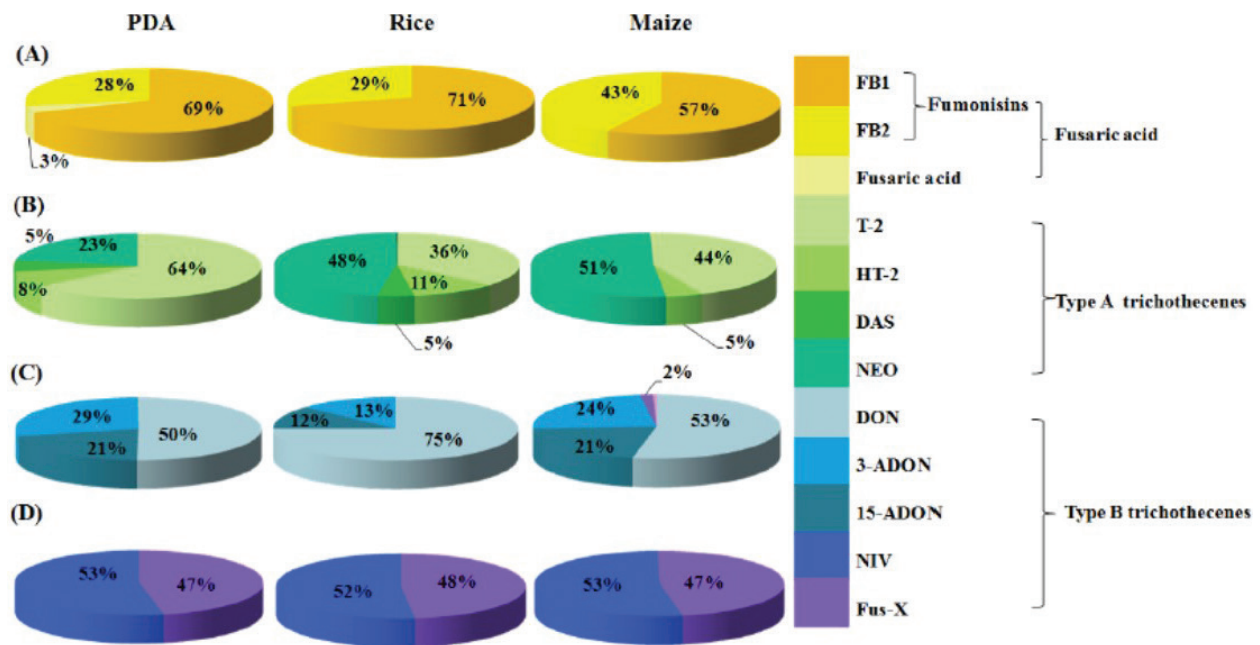


Figure 2. Mycotoxin classification according to main four *Fusarium* species (A) *F. proliferatum* (B) *F. langsethiae* (C) *F. graminearum* and (D) in PDA, rice and maize medium [5].

levels for cereals and cereals products were set in “Commission Recommendation 2013/165/EU” [34]. Maximum limits for DON, ZEA, fumonisins, T-2 and HT-2 toxins have been set for cereals and by-products according to the production technology used [35].

6. Fungal resistance

Resistance of *Fusarium* to antifungal drugs has been defined by many researchers. It is known that many FSSC members cause fusarial onychomycosis [36]. *F. solani* showed more resistance to antifungal agents than others [37]. The effect of azole antifungals used clinically is depend on a particular site, lanosterol-14 α -demethylase. While imidazole or triazole rings are important for conferring the therapeutic effect in animals, epoxiconazole, propiconazole, difenconazole, bromuconazole and tebuconazole are used for plants. *Fusarium* spp. are resistant to azoles [38].

Tupaki-Sreepurna et al. [39] reported that FSSC members, mainly *F. falciforme* and *F. keratoplasticum*, showed multi-drug resistance against caspofungin and azoles. Only a few antifungal agents (voriconazole, posaconazole and amphotericin B) showed *in-vitro* activity against *F. falciforme* and *F. keratoplasticum* [40].

Conversely, the echinocandins are lipopeptide molecules which effectively work by inhibiting 1,3- β -D-glucan synthase of the fungal membrane. If a change occurs in the amino acid residues of β -1,3-glucan synthase enzyme subunits (FKS subunits) in the treatment process, it may lead to increased drug resistance [41, 42].

Polyenes, which are fungicidal, are known as amphipathic drugs, such as nystatin and amphotericin-B. The complexes show efficacy via destroying the proton gradient, allowing for the leakage of ions and removal of ergosterol from phospholipids in the membrane, thus causing fungal cell death in the process [43, 44].

7. Plant disease resistance mechanism

Plants, humans and animals give instant response to the pathogen. In animals, this effect is seen as antibody production, while in plants, it is seen in the form of secretion of various proteins, such as defense-related enzymes and pathogenesis-related proteins [45]. Defense-related enzymes are of great importance in the plant disease resistance mechanism. Immunized plants have rich defense-related enzymes that prevent them from suffering large losses.

If a plant is stimulated by a pathogen, early local defense reactions (a local programmed cell death) are followed by systemic responses (signal is transmitted from infected tissue to the whole plant). At the end, overall defense gene expression gets induced. Consequently, signal perception is essential for plants to combat pathogens [46, 47].

Numerous studies have been done on the transporter genes of plants for improved resistance to *Fusarium* spp. A sucrose transporter gene (IbSWEET10) of the SWEET gene family obtained from the sweet potato line ND98 was tested for this purpose. This overexpression of the gene has been shown to reduce sugar levels and has a potential use to lower carbohydrate levels and increase the resistance of the plant [48].

8. Fungal transporters

Transporters are of great importance in protecting fungi against plant defense compounds. Transporters enable efflux of the plant-originated defense compounds. Although resveratrol (from grape) and camalexin (from *Arabidopsis*) transport via the transporter BcatrB of *Botrytis cinerea*, pisatin (from pea) transports by the NhABC1 transporter of *F. solani* f. sp. *pisi*, and rishitin (from potato) transports via the GpABC1 transporter of *F. sambucinum* [4, 49–51].

Transporters are divided into two major classes: the ATP-binding cassette (ABC) and the major facilitator superfamily (MFS) transporters. ABC transporters are known to be important for resistance against fungal pathogens, particularly for pleiotropic drug resistance or multidrug resistance domains [52]. Although some transporters produce specific or non-specific toxins, some of them show very specific responses to fungicide sensitivity or resistance [53].

9. Identification, control and management

It is possible to identify the genus *Fusarium* by several methods. On culturing, hyaline, banana-shaped and multicellular macroconidia are very common; however, to identify them at the

species level is not easy. Therefore, molecular methods are needed. Some of the most commonly used molecular methods are the genus-specific PCR, 28 s rRNA gene sequencing, sequence-based PCR, multiplex tandem PCR and automated repetitive sequence-based PCR [54].

As a biological control, Ben Amira et al. [55] showed that when *Trichoderma harzianum* was co-cultured with *F. solani*, the former happened to have an antagonistic effect *in-vitro*. Then, they repeated this experiment by inoculating olive tree roots with the same *T. harzianum* and *F. solani* combination. They reported that the former showed a mycoparasitic reaction and antagonistic effects on *F. solani*. Therefore, mycoparasitic fungi, such as *T. harzianum* may be used as a biocontrol agent against *Fusarium*.

Notably, agricultural and chemical precautions cannot be completely successful in preventing *Fusarium*-related diseases in plants [56]. Therefore, synthetic fungicides are not a true approach for preventing the *Fusarium*-related diseases due to their harmful effects on the ecosystem and environment, and growing disease-resistant species to combat *Fusarium*-related diseases seems a more sustainable approach. Resolving the concern of plant diseases caused by *Fusarium* using biological control methods seems to be a more efficient and eco-friendly approach for agricultural products.

Author details

Tulin Askun

Address all correspondence to: taskun@balikesir.edu.tr

Faculty of Sciences and Arts, Department of Biology, University of Balikesir, Balikesir, Turkey

References

- [1] Lamprecht SC, Tewoldemedhin YT, Botha WJ, Calitz FJ. *Fusarium graminearum* species complex associated with maize crowns and roots in the KwaZulu-Natal Province of South Africa. Plant Disease. 2011;**95**:1153-1158. DOI: 10.1094/PDIS-02-11-0083
- [2] Chetouhi C, Bonhomme L, Lasserre-Zuber P, Cambon F, Pelletier S, Renou JP, et al. Transcriptome dynamics of a susceptible wheat upon *Fusarium* head blight reveals that molecular responses to *Fusarium graminearum* infection fit over the grain development processes. Functional & Integrative Genomics. 2016;**16**:183-201. DOI: 10.1007/s10142-016-0476-1
- [3] McMullen M, Bergstrom G, De Wolf E, Dill-macky R, Hershman D, Shaner G, et al. *Fusarium* head blight disease cycle, symptoms, and impact on grain yield and quality frequency and magnitude of epidemics since 1997. Plant Disease. 2012;**96**:1712-1728. DOI: 10.1094/PDIS-03-12-0291-FE©

- [4] Coleman JJ. The *Fusarium solani* species complex: Ubiquitous pathogens of agricultural importance. *Molecular Plant Pathology*. 2016;**17**(2):146-58. DOI: 10.1111/mpp.12289
- [5] Shi W, Tan Y, Wang S, Gardiner D, De Saeger S, Liao Y, et al. Mycotoxigenic potentials of *Fusarium* species in various culture matrices revealed by mycotoxin profiling. *Toxins* (Basel). 2016;**9**:1-15. DOI: 10.3390/toxins9010006
- [6] Thangavelu R, Palaniswami A, Velazhahan R. Mass production of *Trichoderma harzianum* for managing *Fusarium* wilt of banana. *Agriculture, Ecosystems and Environment*. 2004;**103**:259-263. DOI: 10.1016/J.AGEE.2003.09.026
- [7] Stephens AE, Gardiner DM, White RG, Munn AL, Manners JM. Phases of infection and gene expression of *Fusarium graminearum* during crown rot disease of wheat. *Molecular Plant-Microbe Interactions*. 2008;**21**:1571-1581. DOI: 10.1094/MPMI-21-12-1571
- [8] Austen B, McCarthy H, Wilkins B, Smith A, Duncombe A. Fatal disseminated *Fusarium* infection in acute lymphoblastic leukaemia in complete remission. *Journal of Clinical Pathology*. 2001;**54**:488-490. DOI: 10.1136/jcp.54.6.488 Updated
- [9] Mayayo E, Pujol I, Guarro J. Experimental pathogenicity of four opportunist *Fusarium* species in a murine model. *Journal of Medical Microbiology*. 1999;**48**:363-366. DOI: 10.1099/00222615-48-4-363
- [10] Namboothiri PES, Nair S, Vijayan K, Visweswaran V. Disseminated *Fusarium oxysporum* neurospinal infection. *Indian Journal of Orthopaedics*. 2014;**48**(2):220-222. DOI: 10.4103/0019-5413.128773
- [11] Guendouze-Bouchefa N, Madani K, Chibane M, Boulekbache-Makhlouf L, Hauchard D, Kiendrebeogo M, et al. Phenolic compounds, antioxidant and antibacterial activities of three Ericaceae from Algeria. *Industrial Crops and Products*. 2015;**70**:459-466. DOI: 10.1016/j.indcrop.2015.03.053
- [12] Gauthier GM, Keller NP. Crossover fungal pathogens: The biology and pathogenesis of fungi capable of crossing kingdoms to infect plants and humans. *Fungal Genetics and Biology*. 2013;**61**:146-157. DOI: 10.1016/j.fgb.2013.08.016
- [13] Bouhet S, Oswald IP. The effects of mycotoxins, fungal food contaminants, on the intestinal epithelial cell-derived innate immune response. *Veterinary Immunology and Immunopathology*. 2005;**108**:199-209. DOI: 10.1016/j.vetimm.2005.08.010
- [14] Schenk M, Mueller C. The mucosal immune system at the gastrointestinal barrier. *Best Practice & Research. Clinical Gastroenterology*. 2008;**22**:391-409. DOI: 10.1016/j.bpg.2007.11.002
- [15] Devreese M, De Backer P, Croubels S. Overview of the most important mycotoxins for the pig and poultry husbandry. *Vlaams Diergeneeskdt Tijdschr* 2013;**82**:171-180
- [16] Cortinovis C, Pizzo F, Spicer LJ, Caloni F. *Fusarium* mycotoxins: Effects on reproductive function in domestic animals—A review. *Theriogenology*. 2013;**80**:557-564. DOI: 10.1016/j.theriogenology.2013.06.018

- [17] Minervini F, Aquila MED. Zearalenone and reproductive function in farm animals. *International Journal of Molecular Sciences*. 2008;**9**:2570-2584. DOI: 10.3390/ijms9122570
- [18] Weber M, Balogh K, Fodor J, Erdélyi M, Ancsin Z, Mézes M. Effect of T-2 and HT-2 toxin during the growing period on body weight, lipid peroxide and glutathione redox status of broiler chickens. *Acta Veterinaria*. 2010;**79**:27-31. DOI: 10.2754/avb201079010027
- [19] Antonissen G, Martel A, Pasmans F, Ducatelle R, Verbrugghe E, Vandenbroucke V, et al. The impact of *Fusarium* mycotoxins on human and animal host susceptibility to infectious diseases. *Toxins (Basel)*. 2014;**6**:430-452. DOI: 10.3390/toxins6020430
- [20] Quarta A, Mita G, Haidukowski M, Santino A, Mulè G, Visconti A. Assessment of trichothecene chemotypes of *Fusarium culmorum* occurring in Europe. *Food Additives and Contaminants*. 2005;**22**:309-315. DOI: 10.1080/02652030500058361
- [21] Tian Y, Tan Y, Liu N, Liao Y, Sun C, Wang S, et al. Functional agents to biologically control deoxynivalenol contamination in cereal grains. *Frontiers in Microbiology*. 2016;**7**:1-8. DOI: 10.3389/fmicb.2016.00395
- [22] Marcinkowska J. Fungi occurrence on seeds of field pea. *Acta Mycologica*. 2013;**43**:77-89. DOI: 10.5586/am.2008.010
- [23] Ozgonen H, Gulcu M. Determination of mycoflora of pea (*Pisum sativum*) seeds and the effects of *Rhizobium leguminosorum* on fungal pathogens of peas. *African Journal of Biotechnology*. 2011;**10**:6235-6240. DOI: 10.5897/AJB10.2691
- [24] Cheli F, Battaglia D, Gallo R, Dell'Orto V. EU legislation on cereal safety: An update with a focus on mycotoxins. *Food Control*. 2014;**37**:315-325. DOI: 10.1016/j.foodcont.2013.09.059
- [25] Binder EM, Tan LM, Chin LJ, Handl J, Richard J. Worldwide occurrence of mycotoxins in commodities, feeds and feed ingredients. *Animal Feed Science and Technology*. 2007;**137**:265-282. DOI: 10.1016/j.anifeedsci.2007.06.005
- [26] Chehri K, Jahromi ST, Reddy KRN, Abbasi S, Salleh B. Occurrence of *Fusarium* spp. and fumonisins in stored wheat grains marketed in Iran. *Toxins (Basel)*. 2010;**2**:2816-2823. DOI: 10.3390/toxins2122816
- [27] Llamas DP, Patón LG, Díaz MG, Serna JG, Sáez SB. The effects of storage duration, temperature and cultivar on the severity of garlic clove rot caused by *Fusarium proliferatum*. *Postharvest Biology and Technology*. 2013;**78**:34-39. DOI: 10.1016/j.postharvbio.2012.12.003
- [28] Waśkiewicz A, Irzykowska L, Bocianowski J, Karolewski Z, Kostecki M, Weber Z, et al. Occurrence of *Fusarium* fungi and mycotoxins in marketable asparagus spears. *The Polish Journal of Environmental*. 2010;**19**:219-225
- [29] Hsuan HM, Salleh B, Zakaria L. Molecular identification of *Fusarium* species in *Gibberella fujikuroi* species complex from rice, sugarcane and maize from peninsular Malaysia. *International Journal of Molecular Sciences*. 2011;**12**:6722-6732. DOI: 10.3390/ijms12106722

- [30] Gomes LB, Ward TJ, Badiale-Furlong E, Del Ponte EM. Species composition, toxigenic potential and pathogenicity of *Fusarium graminearum* species complex isolates from southern Brazilian rice. *Plant Pathology*. 2015;**64**:980-987. DOI: 10.1111/ppa.12332
- [31] Das IK, Audilakshmi S, Annapurna A, Kannababu N, Patil JV. Relationship among seed germination and other characters associated with fusarium grain mould disease in sorghum (*Sorghum bicolor* L. Moench) using path coefficient analysis. *Canadian Journal of Plant Pathology*. 2012;**34**:203-212. DOI: 10.1080/07060661.2012.689260
- [32] Mukanga M, Derera J, Tongoona P, Laing MD. Farmers ' perceptions and management of maize ear rots and their implications for breeding for resistance. *African Journal of Agricultural Research*. 2011;**6**:4544-4554. DOI: 10.5897/AJAR11.451
- [33] European Commission. Commission recommendation no 2006/576 of 17 August 2006 on the presence of deoxynivalenol, zearalenone, ochratoxin a, T-2 and HT-2 and fumonisins in products intended for animal feeding. *Official Journal of the European Union, L*. 2006;**229**:7-9
- [34] European Commission. Commission recommendation no 2013/165/EU of 27 March 2013 on the presence of T-2 and HT-2 toxin in cereals and cereal products. *Official Journal of the European Union, L*. 2013;**91**:12-15
- [35] European Commission. Commission regulation (EU) 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. *Official Journal of the European Union, L*. 2006;**364**:5-24
- [36] van Diepeningen AD, de Hoog GS. Challenges in *Fusarium*, a trans-kingdom pathogen. *Mycopathologia*. 2016;**181**:161-163. DOI:10.1007/s11046-016-9993-7
- [37] Azor M, Gené J, Cano J, Guarro J. Universal in vitro antifungal resistance of genetic clades of the *Fusarium solani* species complex. *Antimicrobial Agents and Chemotherapy*. 2007;**51**:1500-1503. DOI: 10.1128/AAC.01618-06
- [38] Al-Hatmi AMS, Meis JF, de Hoog GS. *Fusarium*: Molecular diversity and intrinsic drug resistance. *PLoS Pathogens*. 2016;**12**:1-8. DOI:10.1371/journal.ppat.1005464
- [39] Tupaki-Sreepurna A, Al-Hatmi AMS, Kindo AJ, Sundaram M, de Hoog GS. Multidrug-resistant *Fusarium* in keratitis: A clinico-mycological study of keratitis infections in Chennai, India. *Mycoses*. 2017;**60**:230-233. DOI: 10.1111/myc.12578
- [40] Guevara-Suarez M, Cano-Lira JF, Cepero de García MC, Sopo L, De Bedout C, Cano LE, et al. Genotyping of *Fusarium* isolates from onychomycoses in Colombia: Detection of two new species within the *Fusarium solani* species complex and in vitro antifungal susceptibility testing. *Mycopathologia*. 2016;**181**:165-174. DOI: 10.1007/s11046-016-9983-9
- [41] Perlin DS. Current perspectives on echinocandin class drugs. *Acta Mycologica*. 2018;**6**: 19-20. DOI: 10.2217/fmb.11.19

- [42] Parente-Rocha JA, Bailão AM, Amaral AC, Taborda CP, Paccez JD, Borges CL, et al. Antifungal resistance, metabolic routes as drug targets, and new antifungal agents: An overview about endemic dimorphic fungi. *Mediators of Inflammation*. 2017;**2017**: 9870679. DOI: 10.1155/2017/9870679
- [43] Anderson TM, Clay MC, Cioffi AG, Diaz KA, Hisao GS, Tuttle MD, et al. Amphotericin forms an extramembranous and fungicidal sterol sponge. *Nature Chemical Biology*. 2014;**10**:400-406. DOI: 10.1038/nchembio.1496
- [44] Gruszecki WI, Gagoś M, Hereć M, Kernen P. Organization of antibiotic amphotericin B in model lipid membranes. A mini review. *Cellular & Molecular Biology Letters*. 2003;**8**:161-170
- [45] Thakker JN, Patel S, Dhandhukia PC. Induction of defense-related enzymes in banana plants : Effect of live and dead pathogenic strain of *Fusarium oxysporum* f. Sp. Cubense. 2013;**2013**. DOI: 10.1016/j.agee.2003.09.026
- [46] Nürnberger TSD. Signal transmission in the plant immune response. *Trends in Plant Science*. 2018;**6**:372-379
- [47] Thakker JN, Patel S, Dhandhukia PC. Induction of defense-related enzymes in banana plants: Effect of live and dead pathogenic strain of *Fusarium oxysporum* f. Sp. Cubense., *ISRN Biotechnology*. 2013;**2013**:1-6. DOI: 10.5402/2013/601303
- [48] Li Y, Wang Y, Zhang H, Zhang Q, Zhai H, Liu Q, et al. The plasma membrane-localized sucrose transporter IbSWEET10 contributes to the resistance of sweet potato to *Fusarium oxysporum*. *Frontiers in Plant Science*. 2017;**8**:1-15. DOI: 10.3389/fpls.2017.00197
- [49] Wang Y, Lim L, DiGuistini S, Robertson G, Bohlmann J, Breuil C. A specialized ABC efflux transporter GcABC-G1 confers monoterpene resistance to *Grosmannia clavigera*, a bark beetle-associated fungal pathogen of pine trees. *The New Phytologist*. 2013;**197**:886-898. DOI: 10.1111/nph.12063
- [50] Stefanato FL, Abou-Mansour E, Buchala A, Kretschmer M, Mosbach A, Hahn M, et al. The ABC transporter BcatrB from *Botrytis cinerea* exports camalexin and is a virulence factor on *Arabidopsis thaliana*. *The Plant Journal*. 2009;**58**:499-510. DOI: 10.1111/j.1365-3113X.2009.03794.x
- [51] Schoonbeek H, Del Sorbo G, De Waard MA. The ABC transporter BcatrB affects the sensitivity of *Botrytis cinerea* to the Phytoalexin resveratrol and the fungicide Fenpiclonil. *Molecular Plant-Microbe Interactions*. 2001;**14**:562-571. DOI: 10.1094/MPMI.2001.14.4.562
- [52] Kretschmer M, Leroch M, Mosbach A, Walker A-S, Fillinger S, Mernke D, et al. Fungicide-driven evolution and molecular basis of multidrug resistance in field populations of the grey mould fungus *Botrytis cinerea*. *PLoS Pathogens*. 2009;**5**:e1000696. DOI: 10.1371/journal.ppat.1000696
- [53] Del Sorbo G, Schoonbeek H, De Waard MA. Fungal transporters involved in efflux of natural toxic compounds and fungicides. *Fungal Genetics and Biology*. 2000;**30**:1-15. DOI: 10.1006/fgbi.2000.1206

- [54] Tortorano AM, Richardson M, Roilides E, van Diepeningen A, Caira M, Munoz P, et al. ESCMID and ECMM joint guidelines on diagnosis and management of hyalohyphomycosis: *Fusarium* spp., *Scedosporium* spp. and others. *Clinical Microbiology and Infection*. 2014;**20**:27-46. DOI: 10.1111/1469-0691.12465
- [55] Ben Amira M, Lopez D, Triki Mohamed A, Khouaja A, Chaar H, Fumanal B, et al. Beneficial effect of *Trichoderma harzianum* strain Ths97 in biocontrolling *Fusarium solani* causal agent of root rot disease in olive trees. *Biological Control*. 2017;**110**:70-78. DOI: 10.1016/j.biocontrol.2017.04.008
- [56] Lehoczki-Krsjak S, Szabó-Hevér Á, Tóth B, Kótai C, Bartók T, Varga M, et al. Prevention of *Fusarium* mycotoxin contamination by breeding and fungicide application to wheat. *Food Addit Contam Part A*. 2010;**27**:616-628. DOI: 10.1080/19440041003606144