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CHARACTERIZATION OF FEED CONTAMINATION BY *Fusarium* sp. - A REVIEW

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Abstract

Certain Fusarium species and strains are potential producers of three most important classes of mycotoxins: fumonisins (FB1, FB2, FB3); zearalenone (ZEA) and trichothecenes, such as deoxynivalenol (DON), *nivalenol* (NIV), or *HT-2 toxin and T-2 toxin. The ingestion consequences of these fungal compounds can lead to a range from acute to chronic diseases with high morbidity. The use of contaminated feed can have serious effects not only on health, but also on the productive potential of livestock and poultry, with high risk of further mycotoxins spreading in the food chain to the final consumer. Therefore, this paper aimed to present information on the main mycotoxins produced by different species of Fusarium contaminants, focusing on the toxicological effects on farm animals. The effects of each mycotoxin type on ruminants, horses, pigs, and poultry are described.*

Key words*: feed, Fusarium, mycotoxins, livestock, poultry.*

INTRODUCTION

Feed can be classified into groups including forages, cereals, compound feeds, products and by-products from the human food and brewing industry. Animal feed usually includes a combination of elements that must meet nutritional requirements at low cost for a good health. Cereals and cereal-based products are usually the most used ingredients in feed production and contain most of the nutrients useful for animal husbandry (Pereira et al., 2019).

Filamentous fungi are microorganisms that can be found everywhere in nature. Although they mostly live saprophytically or in symbiosis with other living organisms, they can also develop infections and contaminations. In the case of mycotoxigenic fungi, the problem is not limited to their presence and development, but also on the mycotoxin contamination which contribute to the depreciation of infected substrates. The genus *Fusarium* includes some infectious pathogenic species for plants, animals, and humans. The spectrum of mycotoxins produced is very varied, however the most studied are: fumonisins, trichothecenes and zearalenone with a particularly serious impact on human and animal health (Ismaiel & Papenbrock, 2015; Fremy et al., 2019).

In this context, the current review is intended to provide a comprehensive summary on important feed contaminants of *Fusarium* species, their toxic metabolites, and effect of mycotoxin exposure on farm animals.

Fusarium contamination in feed

Mycotoxins are highly stable compounds, and due to their persistence in the food network they are of major concern. Moulds and mycotoxins can contaminate feeds at all stages of production, in the field, before harvesting, and also during storage or processing. The main fungal contaminants able to produce mycotoxins are Aspergillus*, Penicillium, Fusarium, Alternaria* and *Claviceps.* The severity of infection and contamination is dependent on the host plant, climatic conditions and agronomic practices (Gallo et al., 2015). Among mycotoxins, the most common are aflatoxins, ochratoxins, fumonisins, paulin, deoxynivalenol and their derivatives, as well as other trichothecenes. The infiltration of

mycotoxins in the food chain is promoted by both biotic and abiotic factors. Temperature and humidity are of high importance, as they influence the biology and ecology of phytopathogenic fungi. Contamination can also be influenced by technological factors, such as the phytosanitary treatments applied in vegetation for the prevention and plant protection against pest and diseases, time and harvesting methods, and storage conditions (Ponce-García et al., 2018).

The contamination with *Fusarium* spp can occur in the field, spreading in the plant, and eventually, continuing the depreciation during storage. In many cases the fungal infection is not limited to quantitative depreciation, and can be worsened due to the mycotoxin contamination, which reduces the quality of the harvest, or even compromise it.

The *Fusarium* genus comprises around 70 well-known species, and as many as 300 putative species, of which only some regularly contaminate feed (Table 1).

Table 1. Recommendations and regulations for safe limits of *Fusarium* mycotoxin concentrations in grains at the European Union[a] (Munkvold, 2017)

Mycotoxins	Fungal species	Limits of mycotoxines concentration in grains	
		for human food	for animal feed
Deoxynivalenol	*Fusarium graminearum F. culmorum*	750 ppb	1750 ppb
Fumonisins B1, B2, B3	*F. vertillioides F.proliferatum*	1000 ppb	4000 ppb
T-2	*F. acuminatum F. langsethiae, F. sporotrichioides*	50-200 ppb [b]	100-200 ppb[b]
Zearalenone	*F. graminearum F. culmorum*	75-100 ppb[c]	100-350 ppb[d]

Legend: [a]Commission Regulation (EC) No 1126/2007 or 576/2006, [b]Varies among grain types, [c]Varies among specific food items, [d]Varies among livestock species, up to 1000 ppb for oats with husks.

Mycotoxins produced by *Fusarium* species

Mycotoxigenic *Fusarium* species have the ability to produce secondary metabolic compounds with toxic effects on humans and animals, especially when they develop on suitable substrates. These substances are characterized by a low molecular weight that can easily be absorbed, ingested or inhaled, causing a wide range of diseases, even death of humans and animals. Moreover, due to their slow metabolism and increased accumulation risk in the body, their negative effects are more harmful to the host (Ferrigo et al., 2016).

Several hundred compounds have been described as toxic or potentially toxic secondary metabolites of *Fusarium* spp. Toxicity of many of these compounds has been demonstrated in bioassays or feeding studies. In this context, many studies are focused on investigating the short and long term exposure effects to these compounds, either as one or as mycotoxin mixture. Several authors have already shown the dynamics of various toxins within the body, their bioavailability and mechanisms of action according to the species involved (Loiseau et al., 2015).

Among the most important mycotoxins produced by *Fusarium* species are the fumonisin (FB1, FB2, FB3); zearalenone (ZEA) and trichothecene (deoxynivalenol, nivalenol, HT-2 and T-2 toxins), while trichothecenes are potent inhibitors of protein synthesis. They can also produce emerging mycotoxins such as fusoproliferin (FUS), beauvericin (BEA), eniatins, moniliformin (MON), fusaric acid, fusarin AD, gliotoxin, butenolite, which are recently discovered and less studied (Stanciu et al., 2017). Mycotoxins produced by species of *Fusarium* genus have acute toxic effects and chronic effects. Due to these factors, *Fusarium* species are considered among most economically important mycotoxin producing fungi. However, the major problem following the consumption of contaminated products isn't the acute sickness episodes, but rather the ingestion of low amounts of toxins that can cause a number of metabolic, physiological and immunological disorders. Symptoms related to mycotoxicosis can occur when mycotoxins are consumed at very low concentrations, even below the limits of detection (Escrivá et al., 2015).

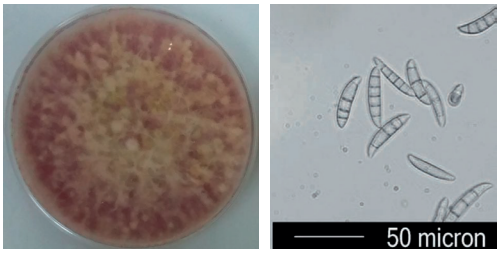
Forage contaminants of *Fusarium* genus

The contamination with *Fusarium* spp can cause plants, animals and humans, diseases / health damages etc. In plants, they have a varied host spectrum. The American Society of Phytopathology estimates that approximately 80% of economically important plant species are affected by *Fusarium* sp. (Moss, 2002). There are many *Fusarium* species that can infect cereals, causing quantitative and/or

qualitative losses to both food and feet grain crops, as well as grasses. For instance, on cereals, the most common phytopathogenic fungi are *F. graminearum, F. culmorum*, *F. avenaceum*, *F. poae* and *F. langsethiae*. Many of these species can be present in soil, as saprophytes, but can become pathogenic, and damage seed, seedlings, mature plants, including the harvest. All cereals are susceptive to the infection, which can be caused either by individual *Fusarium* species, or more commonly, co-occurring species complex (Ferrigo et al., 2016).

Characterization of *Fusarium culmorum*

F. culmorum is associated with stem base rot and ear blight (also known as Fusarium head blight). *In vitro*, colonies are rapidly growing, exceeding 9 cm in diameter after 7 days when incubated on Potato-Dextrose-Agar (PDA) medium. The aerial mycelium is whitish to yellow or tan, while the substrate mycelium and the reverse are carmine to intensely red brown (Figure 1). The optimum temperature for the mycelial growth and sporulation is 20 to 24°C.



a b

Figure 1. *Fusarium culmorum*
a. Colony morphology on PDA (original);
b. macroconidia (Pancaldi et al., 2010).

The main mycotoxins produced by *F. culmorum* include trichothecenes, such as deoxynivalenol (DON), nivalenol (NIV), and T-2 toxin, as well as zearalenone (ZEA) and fusarins (Wagacha & Muthomi, 2007). But the major compound produced is DON, also known as vomitoxin. When animals are fed with contaminated feed by DON , this toxin causes vomiting in animals or feed refusal because the feed is unpalatable., especially to pigs (Amaresan et al., 2020).

Phylogenetically, *F. culmorum* is closely related to *F. graminearum*, with who is sharing similar colony morphology. However, they can be distinguished based on macroconidia morphology, some genetic differences, and secondary metabolites profile (Sirbu et al., 2020).

Characterization of *Fusarium avenaceum*

F. avenaceum forms dense, pale orange aerial mycelium on PDA, becoming pinkish white to white, as the culture ages. The other side of *F. avenaceum* can be peach or pale orange to orange. Some cultures produce a darker red mycelium and a red pigment in the agar, as the cultures are ageing (Figure 2).

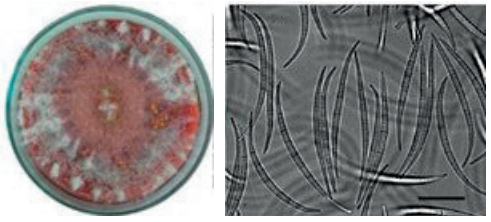


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Figure 2. *Fusarium avenaceum*: a. typical colony morphology on Potato-Sucrose-Agar (after 14 days incubation at 23°C, in dark; b. macroconidia compared to the scale bar of 20 μm (Yli-Mattila et al., 2018)

This fungus is relatively fast growing, the optimum temperature for growth and sporulation being at 20°C. It is found in temperate climates as a saprophyte in the soil but can become a parasite on cereals (such as wheat and barley) and perennial grasses, as well as on vegetables, or carnations.

Characterization of *Fusarium graminearum*

Fusarium graminearum is the anamorph of *Gibberella zeae*. Their colonies grow rapidly, and form dense mycelia of variable colour, from white at the beginning of growth, than pink, as the formation of conidia, turning to reddish-brown with age, with yellow or orange iridescence on the upper mycelium (Figure 3). The optimum temperature range for its growth is between 24-26°C (Dudoiu et al., 2016).

This specie is cosmopolitan, it predominantly infects maize, wheat and barley, but also other annual and perennial grass species (Yli-Mattila et al., 2018). In addition to the quantitative

yield losses, harvested grain sustains qualitative problems of contamination with mycotoxins such as NIV, DON, and ZEA (Tamba-Berehoiu et al., 2012).

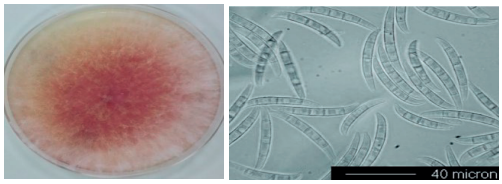

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Figure 3. *Fusarium graminearum*:
a. Colony morphology on PDA after 5 days, at 26°C (original); b. macroconidia (Pancaldi et al., 2010)

Characterisation of *Fusarium poae* species

The aerial mycelium is abundant, and as it forms microconidia, it takes on a powdery appearance. Initially the mycelium is light in colour, but with age darkens to reddish-brown (Figure 4). In the growth medium, it can secrete red (most common) or yellowish pigments. The culture may have a peculiar, sweet odour.

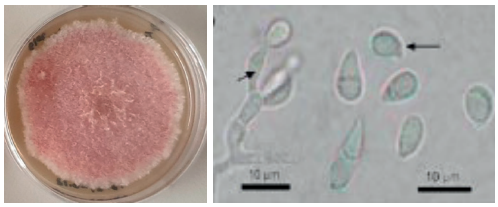

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Figure 4. *F. poae:* a. colony morphology on PDA (original); b. monophialide and microconidia (Morales-Rodríguez et al., 2007).

F. poae is a less important species than *F. graminearum* and *F. culmorum* because this species has been previously considered as a weak pathogen of cereals. although it can infect it. Some isolates of *F. poae* can produce beauvericin, fusarin C, trichothecene diacetoxyscirpenol, nivalenol or T-2 toxin (Pancaldi et al., 2010).

Mycotoxins effect of on animals

Fusarium mycotoxins can induce both acute and chronic toxic effects when ingested. These toxicological effects depend on the mycotoxin type, concentration level, and duration of exposure, exposed animal species and age, as well as other dietary conditions during contamination (Antonissen et al., 2014).

Fumonisins effects on animals

Fumonisins are a class of mycotoxins generally produced by *F. verticillioides* and *F. proliferatum.* However, many other *Fusarium* species are known to produce fumonisinins, but they are of lesser importance in terms of worldwide spread, and incidence in agri-food crops (Bertero et al., 2018).

Among grains, the most contaminated with fumonisinins are maize and maize-based products.

Many fumonisins homologues are known. They are at least 28 types, most of them designed in the A, B, C and P-series. Among these, the B-series is more common and economically important. It includes B1 fumonisin (FB1), which is more studied due to its spread and toxicity impact, followed by B2 fumonisin (FB2) and B3 fumonisin (FB3) (EFSA, 2004). These are commonly found in cereal grains and animal feed, often associated with other mycotoxins. For this reason, the United States Food and Drug Administration (USFDA) has developed certain guidelines which regulates the maximum accepted levels of fumonisin's concentrations in human food and animal feed (USFDA, 2001), ranging from 1 to 50 ppm depending on animal species (Table 2).

Table 2. Fumonisins maximum accepted levels in animal feed as recommended by the US FDA in maize and maize by-products

Animal Class	Maximum Recommended Levels of Total Fumonisins in Maize and Maize By-Products (ppm[1])	Feed Factor[2]	Recommended Maximum of Level of Total Fumonisins in the Total Ration (ppm[1])
Horses[3]	5	0.2	1
Rabbits	5	0.2	1
Catfish	20	0.5	10
Swines	20	0.5	10
Ruminants[4]	60	0.5	30
Mink[5]	60	0.5	30
Poultry[6]	100	0.5	50
Ruminant, Poultry & Mink Breeding Stock[7]	30	0.5	15
All Others[8]	10	0.5	5

Note: [1]Total fumonisins = FB1 + FB2 + FB3; [2] Fraction of maize or maize by-product mixed into the total feed ration; [3]Includes asses, zebras, and onagers; [4] Includes cattle, sheep, goats, and other ruminants that are > 3 months old and fed for slaughter; [5]Fed for pelt production; [6]Includes turkeys, chickens, ducklings and other poultry fed for slaughter; [7]Includes laying hens, roosters, lactating dairy cows and bulls; [8]Includes dogs and cats.

For each animal species the effect of fumonisin B1 can be differ. For example, poultry are defined as less sensitive to fumonisins exposure than pigs and horses, but this does not mean that poultry have immunity against this mycotoxin, or that the presence of fungal toxins in feed does not affect the production of meat and eggs. In 1995, the effects of fumonisins exposure were clearly seen when two-layer farms were seriously affected. The outbreak was characterized by black, sticky diarrhoea. The mortality rate increased to 10%, while egg production decreased by 20%. Overall, only hens are affected when they are exposed to exceptionally high amounts of pollution. Immunosuppression, hepatotoxicity, and nephrotoxicity, as well as a performance reduction, are some of the most evident side effects (Šegvić & Pepeljnjak, 2001).

Horses were found more sensitivity to FB1 toxicity. At concentrations of 0.02 to 0.12 µg/g of feed, FB1 can cause outbreaks, affecting the liver, heart and horses central nervous system. The common manifestations are loss of appetite, weakness, lethargy, allergic reactions, inability to swallow, breading problems, muscle fasciculation, sweating, circling, dilated pupils or absence of a pupillary light reflex (Vendruscolo et al., 2016). In equines, FB1 also induce neurological syndrome and cardiovascular dysfunction (Smith et al., 2002).

Although the fumonisins mechanism of action is not fully understood, it has been shown that in mammalian cells, high concentrations of this mycotoxin alters sphingolipids biosynthesis pathway, which inhibits L-type calcium channels, leading to a decrease in Ca ion release, thus reducing the cardiac activity. Therefore, it can be assumed that leukoencephalomalacia progress may be correlated to a decreased cardiovascular function and damage of the brain vessels (Bertero et al., 2018). Studies on epidermal and dermal cells showed rapidly increase of sphinganine and sphingosine concentrations, associated with disruption of membrane integrity and cell damage (Reisinger et al., 2016). *In vitro* toxicity of FB1 on fresh and frozen semen was also determined. No effects on fresh sperm viability were found after exposure up to 25 µM of B1 fumonisin (Minervini et al., 2010).

Horses and pigs are also very sensitive to fumonisins. In swine, pulmonary edema is one of the typical signs of acute toxicosis triggered by FB1. Pigs sensitivity to fumonisines was seen in several cases of feed contamination, with both *F. verticillioides* or fumonisins fungal metabolites. The main signs were porcine pulmonary edema and reproductive abnormalities, including abortion (Marasas et al., 1988). Due to these observations, several studies were conducted which demonstrate same pulmonary edema caused by B1 fumonisin exposure (Bertero et al., 2018). In swine, as in other species, FB1 causes an inhibition of ceramide synthase (Gumprecht et al., 2001). Hypercholesterolaemia is another sign of FB1 exposure. The necropsy of pigs which died from pulmonary edema, revealed various types of lesions. Beside endothelial lesions, other types of injuries were also described to be caused by chronic intoxication with FB1. Such lesions include basal cell layer dysplasia of the esophagus, sometimes associated with gastric ulceration. These findings also allowed important knowledge for human medicine, as fumonizines ingestion, especially FB1, could be associated with the occurance of human esophageal cancer(Wellington et al., 2000).

Pigs' exposure to FB1 mycotoxin also triggered poor reproductive performance. Therefore, some *in vitro* studies designed to analyse its effect on reproductive functions, using porcine granulosa cell cultures, concluded that at a dose of 10-14 µM the granule cell numbers decreased, but lower doses had no effects. Comparable results have been obtained in other porcine epithelial cell lines and primary cells. On granule cell steroidogenesis, significant effect of FB1 were seen only progesterone production, which was stimulated (Cortinovis et al., 2014).

Ruminants are considerably less sensitive to FB1 compared to monogastric, most likely due to their intestinal microflora activity. However they are not immune to the mycotoxins and can develop biochemical and microscopic liver changes and kidney damage if heavily contaminated feed is consumed. After a prolonged feeding with FB1 contamination, lymphocyte blastogenesis was impaired (Osweiler et al., 1993). Moreover, the short-

chain fatty acids production revealed not to be disturbed by the FB1, therefore neither the ruminal microflora seems to be affected by this mycotoxin (Caloni et al., 2000).

Regarding the reproductive function, FB1 mycotoxin showed no effects on proliferation of granulosa cells and no significant changes on progesterone production. However, at 1 to 3 μM concentrations, the estradiol production seemed to be weakly inhibited (Albonico et al., 2017), thus showing that cattle reproductive function could be affected. But these was not linked to a significant change in CYP19A1 gene expression, as it was seen in porcine granulosa cells by Cortinovis et al. (2014), thus indicating another mechanisms of action that could be involved. *In vitro* studies on the reproductive effects have shown that exposure to multiple mycotoxins plays a key role in cattle and have a strong influence on the entity and type of effects exerted (Albonico et al., 2016; Pizzo et al., 2016).

Deoxynivalenol and its effects on animals

Deoxynivalenol (DON) is the main representative of type B trichothecenes produced by mycotoxigenic *Fusarium* species, most likely by *F. graminearum* and *F. culmorum* but not only (Sobrova et al., 2010). Studies showed that this mycotoxin can contaminate both cereal and their by-products (Bertero et al., 2018). DON seems to inhibit protein synthesis if ingested (Pestka, 2010), and in high doses it can cause emesis, thus also being called as vomitoxin, especially in USA (Wu et al., 2013).

Specific effects of DON in certain animal species sowed that pigs, especially young piglets, are poorly tolerant to this toxin. Absorption and distribution in pigs are generally high, and the excretion is via the urinary and biliary routes. Unlike ruminants, minor metabolism occurs in pigs, and only a limited amount of DON can be detoxified by microflora. The most common signs described in chronically poisoned pigs are reduced feed intake or anorexia due to the stomach and intestine lesions. Other clinical signs also describe lungs and kidneys lesions. Plasma biochemical parameters were also altered (Bertero et al., 2018).

In piglets, DON-contaminated feed altered their innate immune response (Alizadeh et al., 2015) as well as the whole immune system (Pinton et al., 2008), but no clinically relevant impact was observed.

The reproduction system is also affected by DON exposures, even at low and very low doses. At 10 μM of DON, the follicular maturation process was affected, decreasing the follicle reserve and the number of normal follicles (Gerez et al., 2017). Exposed to 0.02 to 2 μM of DON, porcine cumulus-oocyte complexes were either degenerated or dead, with a significant consequence of a reduction in oocytes proportion that reached metaphase stage II (Bertero et al., 2018). Increased number of granulosa cells was reported after 0.034 μM and 0.34 μM DON treatment, with drastic reduction in their number at a dose of 3.4 μM (Ranzenigo et al., 2008). However, the same toxin did not alter bovine granulosa cell proliferation at concentrations between 0.1 and 3.3 μM (Pizzo et al., 2016).

Compared to pigs, cattle are considered less sensitive to DON, due to their metabolism in the rumen, were the microbiota converts it almost completely to a less toxic metabolite called deepoxy-deoxynivalenol (DOM-1). The remains (less than 1%) will be absorbed and find its way into the circulatory system. Although healthy ruminants are less affected due to their intestinal microflora activity, those suffering of acidosis and the young animals could not be able to similarly convert DON in less toxic metabolites, as their ruminal activity is less efficient. Therefore, such animals are considered susceptible to DON toxicosis. The renal route is the main way of excretion as reported by Bertero et al. (2018). The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) identified no obvious adverse effects (NOAEL) for dairy cows and heifers at a dose of 5 to 18 mg DON/kg feed, as no adverse effects on body weight, feed intake or milk production over a 13-week period (EFSA, 2017). Cows fed with DON contaminated feed at 0.59 to 104 mg DON/dry matter concentrate, showed no change in feed intake and total milk yield, while milk fat decreased in relation to mycotoxin concentrations (Daenicke et al., 2011). Although rumen exposure to DON seems

generally resistant, the *in vitro* studies revealed that the reproductive system could be considerably affected by this mycotoxin (Pizzo et al., 2016).

Like cattle species, poultry appear to have a higher tolerance to DON exposure, even at high doses, their performance and productivity revealing no considerably losses. This is considered due to the low level of absorption and rapid metabolism, which helped mycotoxin removal from the plasma (Broekaert et al., 2017). Acute mycotoxicosis, triggered by DON in broiler chickens, has been characterized by extensive under skin haemorrhages, alteration of the nervous system and inflammation of the upper gastrointestinal tract, but only at extremely high contamination, which are unlikely to occur. Regarding egg production, no adverse effects were reported on yield, egg weight and shell thickness (Sypecka et al., 2004). However, the immune system revealed to be sensitive to DON exposure (Awad et al., 2014).

Given the average concentrations of DON in feed it is less likely for this mycotoxin to cause health concern in horses (Bertero et al., 2018).

Zearalenone and effects on animals

Zearalenone (ZEA), is also known as F-2 toxin. Due to their chemical configuration, ZEA and its derivatives are the only known mycotoxins expressing estrogenic effects (King, 2002). ZEA is a lactonic mycotoxin of resorcylic acid produced by several species of *Fusarium*, especially *F. graminearum*. It can be altered in plants, fungi, and animals by phase I and II metabolism. The modified forms of ZEA found in feed include its reduced phase I metabolites (α-zearalenol and β-zearalenol) and its conjugates in phase II (conjugated forms with glucose, sulphate, and glucuronic acid) (Zhang et al., 2018)

The ZEA mycotoxin is commonly found in feed stuffs (Table 3). The maximum recommended values of ZEA concentration in feed stuffs are regulated according to the European Commission Guidance and United Stated Food and Drug Administration Guidance.

Pigs can rapidly absorbed ZEA if fed with contaminated feed; this draws an increased biliary excretion and entero-hepatic circulation. However, the main route of ZEA excretion in pigs is through the urinary tract. Therefore, the metabolic pathway and the amount of ZEA metabolites are the main reasons for different sensitivity to this toxin observed among animal species.

Table 3. Maximum Recommended Levels of ZEA in feed stuffs according to the European Commission Guidance and US Food and Drug Administration Guidance (Dänicke & Winkler, 2015)

Item	Livestock categories		ZEN (μg/kg)
EU	Poultry		-
	Swine	Sows and fattening pigs	250
		Piglets and gilts	100
	Ruminants		500
FDA	Poultry		No guidance levels
	Swine	Sows and fattening pigs	
		Piglets and gilts	
	Ruminants		

Due to the strong estrogenic activity, ZEA and its derivatives are able alter the reproductive system, acting as an endocrine disruptor (Denli et al., 2017). The induced estrogenic effects are hyperestrogenism, anesthesia, ovarian atrophy, and changes in the endometrium (Bertero et al., 2018). The zearalenone effects depend on several factors: the reproductive status of the animal (prepubertal, cyclist or pregnant), as well as the administration time and dose (Holda & Glogowski, 2014).

Unlike monogastric, ruminants are less sensitive to zearalenone toxicity (Pizzo et al., 2016). ZEA is converted to α- and β-zearalenol and not only by hepatic biotransformation, but also by the rumen protozoa. However, young animals are having a less effective ruminal microflora compared to mature cattle, which make calves and young heifers more sensitive. Clinical signs due to ingestion of zearalenone are very rare and occur only in highly contaminated feed or after prolonged exposure. Due to the estrogenic effect, α-zearalanol is used in some countries as a growth-promoting agent in cattle (Thevis et al., 2011). Studies on α- and β-zearalenol impact on follicular cell function showed they may affect the proliferation and steroidogenesis of bovine granular cells. In addition to supporting the ovarian effect of zearalenone, sheep fed this mycotoxin (3-24 mg/sheep/day) have been shown to significantly reduce their ovulation rates during estrus (Pizzo et al., 2016).

Pigs are considered the most sensitive species, and ZEA has various harmful effects on their health, causing reproductive disorders, increasing oxidative stress, decreased digestibility of nutrients, while reducing the growth rate. The high sensitivity of this species is considered to be related to zearalenone convertion into α-zearalenol, which has a higher estrogenic effect than its parent compound, or β-zearalenol. At 1 to 5 ppm, ZEA can induce in young sows, vulvar edema and hyperemia, even vaginal or rectal prolapse, while in adult animals, at various stages of their oestrous cycle, nymphomania, ovarian atrophy, and endometrium changes are more common (Bertero et al., 2016). Adverse oestrus effects in pigs are also reported by Dai et al. (2016), symptoms being related to the dose and oestrus stage in which the mycotoxin is consumed. The effects of α and β-zearalenone on pig oocytes showed a significant decrease in their maturation rate when exposed to 7.5 μM α-zearalenol for two days, compared to 30 μM of β-zearalenol (Alm et al., 2002). Beside the estrogenic syndrome in pigs, that targets the reproductive tract, the mycotoxic effects are also seen at the mammary gland (Minervini & Dell'Aquila, 2008).

ZEA effects on horses were studied mostly *in vitro*, where it was seen that zearalenone is mainly biotransformed to α-zearalenol, than β-zearalenol, which was two to three-fold lower (Bertero et al., 2018). However, recent studies, demonstrated that ZEA induces severe reproductive disorders in both mares and stallions (Dänicke et al., 2021).

In poultry feed, ZEA is a commonly found mycotoxin. Due to the structural similarity to estrogen, ZEA lead to hyperestrogenism resulting in decreased reproductive performance in poultry. In broiler and leghorn chickens ZEA affects the reproductive system (Chi et al., 1980). It also affects egg quality and can increase embryo mortality resulting in reduced hatchability (Liu & Applegate, 2020).

In fish in addition to hepatotoxic, genotoxic, haematological, and reproduction effects (Pietsch et al., 2015), ZEA is also affecting the expression of several genes involved in the regulation of the immune system (Pietsch, 2017).

T-2 and HT-2 toxins and their effects on animals

T-2 and HT-2 toxins belonging to the type A group of trichothecene, which are produced by various *Fusarium* species predominantly by *F. sporotrichioides.* Contamination can occur mainly in cereals, either in field or during storage. The T-2 toxin production seems to be stimulated by the presence of other contaminants, such as *Aspergillus* and *Penicillium* genera (Köpke eta al., 2007). The toxicity of T-2 and its deacetylated form HT-2 toxin is influenced by various factors, such as livestock category, exposure and dosage, animal age, sex, and general physical condition, as well as simultaneous exposure to other mycotoxins (Stoev et al., 2010).

Ruminants are considered less sensitive to the T-2 toxin. As in the case of other mycotoxins, the negative effects of T-2 toxin are significantly diminished by rumen activity. However, younger animals could experience bloody feces and ulcers if exposed to high amounts or prolong feeding with T-2 and HT-2 toxins, as their incipient microflora is less is efficient in detoxification. To sheep, the T-2 toxin reduces the reproductive performance (Bertero et al., 2018). T-2 toxin effects also reduce the reproductive performance in pigs, this animal category being among the most sensitive among all livestock. Immunological and / or haematological effects were noticed at 0.03 mg T-2 toxin/kg/day. Prolonged pigs' feeding with T-2 toxin contaminated forage results in anorexia, and damages of the oral cavity and esophagus. As T-2 toxin inhibits protein synthesis, the immune response and antibody production are also affected. *In vitro* studies indicate that T-2 toxin may alter the growth of granular cell layer and steroidogenesis, proportional to the tested dose (Caloni et al., 2009). Other studies performed on porcine oocytes confirmed the potential of HT-2 and T-2 toxins to disturb the reproductive performance of pigs (Xu et al., 2021).

In poultry, T-2 toxin is rapidly absorbed into the intestinal tract of chickens, then metabolized and eliminated almost completely (approximately 90%) in a single day, although at prolong exposure toxic effects arise (Young et al., 2007), inducing genotoxic, cytotoxic, and immunomodulatory effects, as well as several

disorders at the digestive system, liver, nervous system and skin. The first signs of T-2 toxicosis are the lower feed intake, reduced weight gain and growth retardation, or lower egg production. The eggs collected from T-2 exposed poultry revealed a reduced weight, thinner eggshells and decreased hatching percentage. The lethal dose of T-2 toxin was noticed at approximately 10 mg/kg body weight of chickens, during a seven-day feeding period (Young et al., 2007). Other symptoms of T-2 toxin poisoning reported in poultry include some neurological signs, leukopenia, oral lesions, cyanosis of the comb, depigmentation of the feet's skin and feather alterations.

On horses, there are only few information regarding T-2 toxicosis. Older research results suggest altered locomotion and animal death after one month exposure. Blood biochemistry revealed leucocytosis and anemia. Prolong exposure revealed skin lesions and liver degeneration (Gabal et al., 1986). More recent studies indicated an increased incidence of colic in horses when exposed to DON and T-2 toxins (Caloni & Cortinovis, 2010). In racehorses, it is a strong belief that mycotoxins exposure, even at low levels, can negatively affect to their performance or breeding activities, although no such signs have been reported (Newman & Raymond, 2005).

CONCLUSIONS

Fusarium is one of the most economically important fungal genera due to its mycotoxigenic potential additionally to its' pathogenicity on a wide host variety. *Fusarium* infections significantly reduce plant yields and quality, and make harvest and by-products unsuitable for marketing, due to mycotoxin contamination of food and feed products. The spectrum of mycotoxins is varied, all causing serious negative impact on human and animal health. Mycotoxigenic *Fusarium* species are capable of producing three of the most important classes of mycotoxins, such as fumonisins, zearalenone, and trichothecene. If ingested, such toxins can produce acute and chronic effects in humans and animals following consumption. Pigs are among the most affected livestock, while ruminants are considered less sensitive, thanks to the metabolism of rumen microbiota. Poultry however are affected on prolong exposure.

Regarding other *Fusarium* mycotoxins, such as eniatins and beauvericin, the toxic profile is not fully understood, despite the emerging interest in it, thus being a challenge for future toxicological studies to be performed.

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