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# Relevance of the *Fusarium* toxins deoxynivalenol and zearalenone in ruminant nutrition. A review

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ABSTRACT

Deoxynivalenol (DON) and zearalenone (ZON) produced by *Fusarium* species are agriculturally important mycotoxins of relevance to livestock health. While ZON is known to cause oestrogenic syndromes in animals, a moderate ingestion of DON is associated with reduced performance and immune function. Among farm animals, ruminants appear to have a higher tolerance towards the effects of DON and ZON. As a consequence, feed producers may allocate cereals and roughages which appear contaminated with *Fusarium* toxins to ruminants. In combination with enhanced toxin concentrations during so-called *Fusarium* years, the possible effects in ruminants cannot be overlooked. However, only limited and inconsistent literature data are available about the effects of DON and ZON on ruminants. On the basis of the literature, the kinetics, biotransformation and carry over, as well as the effects of DON and ZON on ruminants, are reviewed. Furthermore, dosage and duration of toxin exposure as well as genetic and physiological factors of ruminants which could influence the variability of the toxin effects are considered and discussed. It is concluded that additional research is needed to study the effects of DON and ZON on ruminants, especially in lactating dairy cows.

KEY WORDS: deoxynivalenol, zearalenone, ruminants

## INTRODUCTION

Mycotoxins are a diverse group of toxic secondary metabolites produced by a wide range of filamentous fungi. It is assumed that more than 300 chemically different mycotoxins exist, formed by more than 350 fungal species (Steyn, 1998). With regard to the occurrence of mycotoxins in feedstuffs, three genera of fungi may be considered to be of particular importance: *Aspergillus*, *Penicillium* and *Fusarium* (Bauer, 2000). Among these the moulds of the genus *Fusarium* are the most important under agricultural conditions in Central Europe (Lew, 1995).

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*Fusaria* are traditionally considered so-called field flora, because these plant pathogens can infect grains at the flowering period and accumulate toxins during the vegetation stage (Bottalico, 1998). The most important *Fusarium* toxins from the point of view of animal health and productivity are DON and ZON (D'Mello et al., 1999). These toxins are most commonly found in Europe, predominantly produced by *Fusarium culmorum* and *Fusarium graminearum* (Bottalico and Perrone, 2002). Especially in years with unfavourable climatic conditions (periods of warm weather with persistent wetness; Sutton, 1982; Oldenburg et al., 2000), the contamination of cereal grains and maize plants with *Fusarium* species can cause considerable agricultural problems resulting in yield loss, quality loss and mycotoxin contamination. With regard to a preventive consumer protection, the carry over of the mycotoxins in animal-derived food products has to be considered.

Numerous investigations on the natural occurrence of *Fusarium* toxins in cereals and forage crops have been carried out during the past years (Tables 1 and 2). It is conspicuous that crop years with higher maximum and mean DON as well as ZON concentrations occur repeatedly (Oldenburg et al., 2000). Due to the high proportion of cereals, as well as forage crops such as maize and grass silage, hay and straw in ruminant diets, both concentrate feeds and basic rations can contribute to the daily toxin exposure of ruminants (Scudamore and Livesey, 1998). Furthermore, since ruminants are regarded as relatively resistant to DON and ZON compared with monogastric animals such as pigs, feed manufacturers will feed cereals which appear contaminated with *Fusarium* toxins primarily to ruminants rather than to pigs. In combination with higher DON and ZON concentrations in cereals and roughages during so called *Fusarium* years, possible mycotoxin effects in ruminants should not be underestimated (Oldenburg et al., 2000; Dänicke et al., 2002a).

Generally, the higher tolerance of ruminants to DON and ZON is attributed to the potential of rumen microbes for metabolization of these toxins. However, up to now these effects were only proved in some *in vitro* investigations with incubated rumen fluid. Only a limited number of corresponding *in vivo* studies, especially with lactating dairy cows, are available and were mainly focussed on pharmacokinetic aspects. Further literature data about the effects of DON and ZON contaminated feedstuffs on the health and performance of ruminants and on nutrient digestibility are relatively rare. Because mostly only case or field reports as well as studies with a limited number of animals and rather short experimental periods were given (for reviews see Hölthershinken et al., 1996; Whitlow and Hagler, 1999; Bauer, 2000; Dänicke et al., 2000) the described effects of DON and ZON on ruminants are not always consistent between the different studies.

The purpose of this article is to summarize the actual state of knowledge regarding the kinetics, biotransformation and carry over of the *Fusarium* toxins DON and ZON in ruminants considering their mode of action. Furthermore, the effects of DON and ZON in dependence of toxin exposure on ruminant health

TABLE 1

Deoxynivalenol (DON) and zearalenone (ZON) concentrations in silo maize, grain maize, silages, hay and grass (according to Oldenburg et al., 2000)

| Cereal type | Year | Toxin | n, positive % | Concentration, mg/kg | | Literature |
|---|---|---|---|---|---|---|
| | | | | range | mean, positive samples | |
| Silo maize[1] | 1995 | | | | | Oldenburg et al., 1996 |
| rest plant | | ZON | 298 (98) | 0.005 - 2.97 | 0.39 | |
| | | DON | 60 (92) | 0.12 - 3.51 | 1.13 | |
| ear | | ZON | 170 (8) | 0.009 - 0.17 | 0.05 | |
| Silo maize[1] | 1996 | | | | | Oldenburg et al., 1997 |
| rest plant | | ZON | 299 (76) | 0.006 - 0.82 | 0.06 | |
| | | DON | 58 (100) | 0.73 - 12.39 | 4.07 | |
| ear | | ZON | 100 (16) | 0.007 - 0.10 | 0.03 | |
| Silo maize[2] | | | | | | Lew et al., 1997 |
| leaves | | DON | 6 (83) | 0.26 - 2.55 | 0.93 | |
| stem | | DON | 6 (100) | 3.25 - 13.75 | 8.69 | |
| Silo maize[3] | 2000 | | | | | Oldenburg and Höppner, 2003 |
| | | DON | 196 (34-86) | 5.91 - 12.00* | 1.1 - 1.44* | |
| Silo maize[4] | 1998-2001 | DON | 4-28 (3-19) | max. 4.64* | 0.43* | Steinhöfel, 2002 |
| | | ZON | 4-28 (3-24) | max. 3.44* | 0.10* | |
| Grain maize[5] | Probably | DON | 10 (80) | max. 0.91 | 0.55 | Usleber et al., 1998 |
| | 1996/1997 | ZON | 10 (80) | max. 0.09 | 0.06 | |
| Ear[6] | 1996 | DON | 85 (95) | max. 2.44 | 0.73 | Ellend et al., 1998 |
| | | ZON | 85 (70) | max. 0.75 | 0.13 | |
| | 1997 | DON | 98 (44) | max. 1.56 | 0.40 | |
| | | ZON | 98 (12) | max. 0.90 | 0.19 | |
| Ear/grain maize[7] | 1998 | DON | 21 (67) | max. 8.95 | 1.74 | Reutter, 1999 |
| | | ZON | 21 (95) | max. 26.00 | 3.36 | |
| Maize silage[8] | | ZON | | | 0.042 | Lepom and Weise, 1989 |
| Maize silage[9] | | ZON | 33 (12) | 0.10 - 4.00* | | Drochner et al., 1984 |
| Maize silage | | ZON | | | 0.005 | Schuh and Baumgartner, 1988 |

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TABLE 1 continued

| Cereal type | Year | Toxin | n, positive % | Concentration, mg/kg | | Literature |
|---|---|---|---|---|---|---|
| | | | | range | mean, positive samples | |
| Maize silage[10] | | ZON | 19 (89) | 0.02 - 0.12* | 0.05* | Valenta and Oldenburg, 1995 |
| Maize silage[11] | | ZON | 25 (84) | 0.01 - 0.17* | 0.05* | |
| Maize silage[12] | 1998 | ZON | 24 (96) | max. 1.07 | 0.13 | Reutter, 1999 |
| | | DON | 24 (79) | max. 9.86 | 1.61 | |
| Grain-maize silage | | ZON | | 0.05 | | Thalmann, 1986 |
| Grain-maize silage | | DON | | 0.015 | | Schuh and Baumgartner, 1988 |
| Grain-maize silage[13] | | DON | | max. 5.30 | | Lepom, 1988 |
| Green-maize silage[13] | | DON | | max. 2.30 | | Lepom, 1988 |
| Grass silage | | ZON | | 0.001 | | Schuh/Baumgartner, 1988 |
| Freshly grass and grass silage[13] | | ZON | | 0.01 - 1.86* | | Engels and Krämer, 1996 |
| Grass[14] | | | | | | Engels and Krämer, 1996 |
| *Lolium perenne* *Lolium multiflorum* | 1991-1992 | ZON | | 0.01- 4.75* | | |
| Hay[15] | | | | | | Oldenburg, 1999 |
| intensiv | 1997 | DON | 9 (100) | 0.23 - 0.72* | 0.46* | |
| extensiv | | DON | 55 (100) | 0.24 - 1.07* | 0.53* | |
| intensiv | | ZON | 9 (100) | 0.005 - 0.08* | 0.02* | |
| extensiv | | ZON | 55 (100) | 0.005 - 0.22* | 0.02* | |
| Soyabean meal[16] | 1999 | ZON | 51 (23) | max. 0.018* | | Valenta et al., 2002 |

* applied on DM (µg/kg), max. = maximum

1. 20 sorts (conventional and "stay green") of 5 locations in Germany (Lower Saxony, North Rhine-Westphalia, Saxony-Anhalt, Bavaria), 2. Samples of Austria, only maize plants with stem rot, 3. Samples from sort trials, 11 locations in 6 German states, 4. Samples of Saxony, Germany, 5. Samples to intent for human nutrition from the German market, origin unknown, 6. Samples to intent for pigs nutrition, Austria, 7. Samples from Schleswig-Holstein, Germany, 8. Sample of the cutting surface of a horizontal silo in Paulinaue/Germany, 9. Samples sent to the Institute for Animal Nutrition at the Tierärztliche Hochschule Hannover, Germany, 10. Samples from Lower Saxony, Germany, 11. Samples of different locations from Lower Saxony and Bavaria, Germany, 12. Samples from Schleswig Holstein, Germany, 13. Samples from Germany, 14. Samples from sort trials, 28 sorts from experimentation areas in North Rhine-Westphalia, Germany, 15. Praxis samples from Germany (North Rhine-Westphalia, Lower Saxony, Hesse, Baden Wuerttemberg, Mecklenburg-Western Pomerania), 16. Samples from the feedstuff industry in Germany

TABLE 2

Deoxynivalenol (DON) and zearalenone (ZON) concentrations in wheat from Germany (according to Oldenburg et al., 2000)

| Cereal type | Year | Toxin | n, positive % | Concentration, mg/kg | | Literature |
|---|---|---|---|---|---|---|
| | | | | range | mean, positive samples | |
| Wheat[1] | 1987 | DON | 84 (96) | 0.004 - 20.54 | 1.69 | Müller et al., 1997 |
| | | ZON | 84 (80) | 0.001 - 8.04 | 0.18 | |
| | 1989 | DON | 78 (69) | 0.003 - 1.19 | 0.15 | |
| | | ZON | 78 (14) | 0.001 - 0.01 | 0.003 | |
| | 1990 | DON | 80 (96) | 0.008 - 8.97 | 0.595 | |
| | | ZON | 80 (11) | 0.001 - 0.015 | 0.005 | |
| | 1992 | DON | 78 (95) | 0.02 - 5.41 | 0.340 | |
| | | ZON | 78 (19) | 0.001 - 0.02 | 0.004 | |
| Wheat, conventional[2] | 1995 | DON | 51 (88) | 0.10 - 1.20 | 0.42 | Marx et al., 1995 |
| | | ZON | 51 (16) | 0.001 - 0.02 | 0.006 | |
| Wheat[3] | 1996 | DON | 21 (90) | 0.14 - 2.84* | 0.76* | Kuhlmann et al., 1999 |
| | | ZON | 21 (62) | 0.003 - 0.22* | 0.04* | |
| Wheat [3] | 1998 | DON | 150 (71) | 0.11 - 11.08* | 1.410* | Döll et al., 2002 |
| | | ZON | 135 (7) | 0.02 - 0.25* | 0.07* | |
| Wheat[4] | 1998 | DON | 116 (86) | max. 10.80 | 2.70 | Reutter, 1999 |
| | | ZON | 125 (74) | max. 0.35 | 0.07 | |
| Wheat, conventional[3] | 2000 | DON | (55) | max. 4.60 | 0.33 | Kirchheim, 2002 |
| | 2001 | DON | (40) | max. 1.90 | 0.28 | |
| Wheat[4] | 2001 | DON | 75 (84) | max. 2.40 | 0.17 | Reutter, 2002 |
| | | ZON | 79 (42) | max. 0.379 | 0.019 | |
| Wheat, conventional[3] | 2002 | DON | | max. 4.90 | 0.500 | Kirchheim, 2003 |
| Wheat[5] | 2002 | DON | 116 | 0.10 - 8.70 | 1.24 | LUFA Nord-West, 2002 |
| | | ZON | 106 | 0.10 - 0.97 | 0.092 | |

* applied on DM (µg/kg) 1. Samples of Baden-Wuerttemberg, 2. Samples of Bavaria, 3. Samples of Thuringia, 4. Samples of Schleswig-Holstein, 5. LUFA Nord-West

and performance, as well as factors which could influence the variability of toxin effects and the carry over are discussed.

## MODE OF ACTION

### *Trichothecenes including deoxynivalenol*

DON (3α, 7α, 15-trihydroxy-12, 13-epoxytrichothec-9-ene-8-one) belongs chemically to the trichothecenes, which comprise a family of 170 closely related sesquiterpenoids (Langseth et al., 2001; Figure 1). Trichothecenes possess a basic and tetracyclic structure which includes a six member oxygen-containing ring, an epoxide in the C-12, 13 position and an olefinic bond in the C-9, 10 position (Betina, 1989). Wide differences in biological activity exist among the several trichothecenes, which is determined by the chemical structure (Betina, 1989).

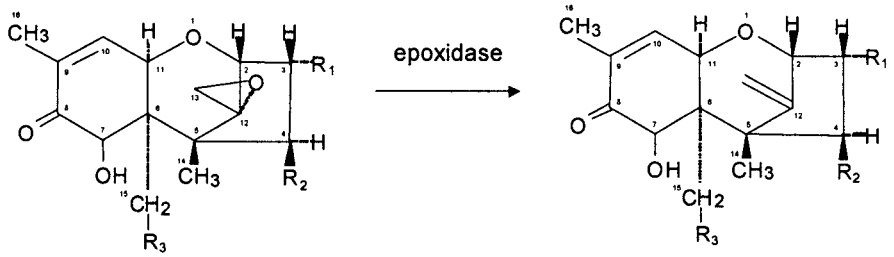


Figure 1. Deepoxidation of trichothecenes to de-epoxy trichothecenes (King et al., 1984)

According to the structural features, trichothecenes can be divided into types A, B, C and D (Ueno, 1985; Rotter et al., 1996). Type A is characterized by a lack of the functional ketone group at C-8 and includes T-2 toxin (T2), T2-tetraol, T2-triol, HT-2 toxin (HT2), diacetoxyscirpenol (DAS), neosolaniol (NEO), monoacetoxyscirpenol (MAS), scirpentriol (Bottalico, 1998). Type B has a carbonyl group at C-8 and is represented by DON, nivalenol (NIV), fusarenon-X (FUS-X), 15-acetyldeoxynivalenol (15-AcDON) and 3-acetyldeoxynivalenol (3-AcDON). Type C is characterized by a second epoxy group at C-7, 8 or C-9, 10 and includes crotocin, and type D is characterized by a macrocyclic ring between C-4 and C-15 and includes derivates of verrucarins and verrucarol.

The basic mechanism of trichothecenes is the inhibition of the protein synthesis at the ribosomal level (Feinberg and McLaughlin, 1989). They bind to the 60S subunit of eukaryotic ribosomes and inhibit the peptidyl transferase activity. Type B trichothecenes including DON are capable of blocking translation at the elongation stage. Moreover, number and positions of substituents at the molecule modify the inhibitory properties (Betina, 1989). The presence of an intact C-9, 10 double bond

and the C-12, 13 epoxide is required for the inhibitory effect, while reduction of the epoxide ring (deepoxidation) results in loss of any apparent toxicity (McLaughlin et al., 1977; Ehrlich and Diagle, 1987; Figure 1). Such a detoxification occurs for DON that is de-epoxidised to the non-toxic metabolite de-epoxy DON as shown for rumen microbes (King et al., 1984).

*Zearalenone*

ZON is chemically described as 6-(10-hydroxy-6-oxo-*trans*-1-undecenyl)-*β*-resorcyclic acid lactone with the molecular formula $C_{18}H_{22}O_5$ (Figure 2). It was given the trivial name zearalenone as a combination of the fragments coming from *Gibberella zeae*, resorcyclic acid lactone, -ene (for the presence of the C-1` to C-2 double bond) and - one, for the C-6` ketone (Urry et al., 1966).

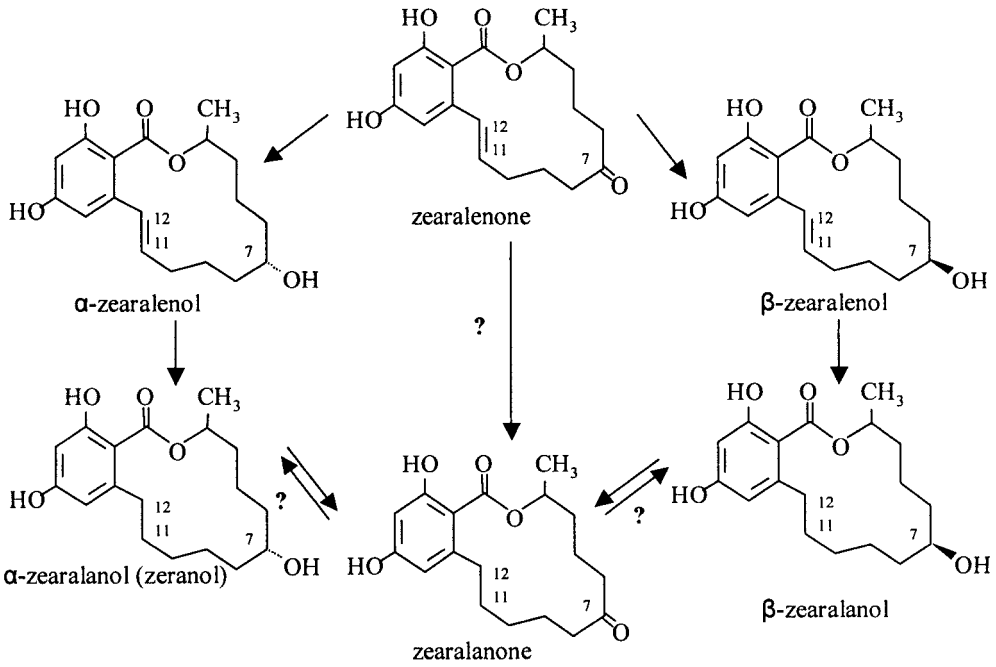


Figure 2. Proposed relationship between routes of zearalenone and its metabolites (Kleinova et al., 2002)

ZON is a non-steroidal mycotoxin, which possesses - beside the anabolic mode of action - primarily oestrogenic properties (Kuiper-Goodman et al., 1987; Figure 2). The reduced products α-zearalenol (α-ZOL) and β-zearalenol (β-ZOL) are the primary metabolites of ZON (IARC, 1993), further derivates are zearalanone (ZAN), zeranol (α-ZAL) and taleranol (β-ZAL; Figure 2).

ZON and its derivates induce oestrogenic effects which are mediated *via* a competitive binding to the cytosolic oestrogen receptor. The receptor-toxin-complex is rapidly transferred into the nucleus, where it binds to specific nuclear receptors and generates oestrogenic responses *via* gene activation, resulting in the production of mRNAs that code for proteins that are normally expressed by receptor-oestrogen complex binding (Riley, 1998). Values for oestrogen receptor binding in target tissues and cells relative to oestradiol of ZON range between < 0.01- 0.1, whereas the relative binding affinities to rat uterine cytoplasmatic receptor for ZON and derivates were α-ZAL > α-ZOL > β-ZAL > ZON > β-ZOL (Tashiro et al., 1980; Kuiper-Goodman et al., 1987; Eriksen and Alexander, 1998). Furthermore, Fitzpatrick et al. (1989) showed that considerable differences in the affinity of α-ZOL to the oestrogen receptor exist between different animal species. Moreover, the relative oestrogenic potencies appear to closely parallel to the relative binding affinity of ZON and its derivates for the uterine cytoplasmic receptor in rodents (Pathre and Mirocha, 1976). Ueno and Tashiro (1981) reported the order of potencies to be α-ZAL > α-ZOL > β-ZAL > ZON > β-ZOL. Thus, α-ZOL is about 3-4 times more oestrogenic than ZON, however β-ZOL is generally less active (Hagler et al., 1980). Consequently, the reduction of ZON to α-ZOL involves an activation of the toxin, while the reduction to β-ZOL possibly means the contrary (Olsen et al., 1989).

## KINETICS, BIOTRANSFORMATION AND CARRY OVER

### *Deoxynivalenol*

Literature data concerning the kinetic behaviour of DON in ruminants are relative rare (Table 3). Prelusky et al. (1984) administered a single oral dose of DON at levels of 1.7 mg/kg body weight (BW) to dairy cows and reported an absorption of approximately 0.6% of the parent toxin. Maximum serum levels of free and conjugated DON for two dosed cows were 200 and 90 ng/ml occurring at 4.7 and 3.5 h after dosing. Only traces (< 2 ng/ml) were detectable 24 h after DON administration. 24-46% of the total DON level in serum occurred as the ß-glucuronide conjugate. Lower oral DON doses of 0.1 mg/kg BW were not detectable in serum. In a study by Cote et al. (1986) dairy cows were fed a DON spiked diet (average 66 mg/kg diet) for five days. 20% of DON fed was recovered in similar proportions as the unconjugated metabolites in the urine (11%) and faeces (9%), whereby the ratio of DON and de-epoxy DON was 1 to 24. After incubation of urine with ß-glucuronidase, concentration of DON and de-epoxy DON increased 1.6 to 3-fold and 7 to 15-fold, respectively, which indicates that the most DON consumed was eliminated in the urine as de-epoxy DON conjugate.

TABLE 3

Deoxynivalenol (DON) dose and DON and metabolites in serum, bile, urine, duodenum and faeces of ruminants

| Animal species | Dose mg/kg diet | Duration day | Deoxynivalenol and its metabolites in serum, urine, bile and duodenal chymus | | Literature |
|---|---|---|---|---|---|
| | | | tissue | concentration and distribution of DON and metabolites | |
| Dairy cow | 50 mg/animal p.o. | Single dose | Serum | DON < DL | Prelusky et al., 1984 |
| | 920 mg/animal p.o. | Single dose | Serum | Total DON levels:<br>$t_{max}/C_{max}$: 4.7 and 3.5 h (post dosing)/200 and 90 ng/ml<br>DON: 24 h (post dosing) < 2 ng/ml<br>→ of the total serum DON:<br>DON (conjugated) 24-46% | |
| Sheep | 5 mg/kg BW p.o. | Single dose | Serum | Total DON levels:<br>$t_{max}/C_{max}$: 4.0-5.3 h (post dosing) = 470-760 ng/ml<br>Complete elimination of DON: 20-30 h (post dosing)<br>→ of the total serum DON:<br>DON (free) 14-37 %<br>DON (conjugated) 63-86 %<br>De-epoxy DON 1.8-2.8 % | Prelusky et al., 1985 |
| | 0.5 mg/kg BW i.v. | Single dose | Serum | $t_{max}/C_{max}$ DON (conjugated): 1.0-1.3 h (post dosing) = 240-520 ng/ml<br>DON (conjugated and free): 7 h (post dosing) = trace levels<br>→ of the total serum DON:<br>DON (conjugated) 15-23%<br>De-epoxy DON 1.4-1.7% | |
| Dairy cow | 66 | 5 | Urine and faeces | De-epoxy DON (unconjugated): up to 72 h = trace levels<br>→ excretion of total DON:<br>DON (unconjugated) and de-epoxy DON (unconjugated) 20% | Cote et al., 1986 |
| Sheep | 5 mg/kg BW p.o. | Single dose | Urine | DON (free and conjugated) and de-epoxy DON (conjugated)<br>$t_{max}$: 6-9 h (post dosing)<br>De-epoxy DON (conjugated): 28-30 h (post dosing) = trace levels | Prelusky et al., 1986 |

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TABLE 3 continued

| Animal species | Dose mg/kg diet | Duration day | Deoxynivalenol and its metabolites in serum, urine, bile and duodenal chymus | | Literature |
|---|---|---|---|---|---|
| | | | tissue | concentration and distribution of DON and metabolites | |
| | | | | → recovery of administered DON: 7.0%<br>DON (free) 2.1%<br>DON (conjugated) 3.6%<br>De-epoxy DON (free) 0.06%<br>De-epoxy DON (conjugated) 1.2% | |
| | | | Bile | De-epoxy DON (conjugated)<br>$t_{max}$: 1-3 h (post dosing) | |
| | | | | → recovery of administered DON: 0.1% | |
| | | | Faeces | → recovery of administered DON: 54-75% | |
| | 0.5 mg/kg BW i.v | Single dose | Urine | DON (free and conjugated) and de-epoxy DON (conjugated)<br>$C_{max}$: 0.33-0.75 h and 0.50-1.5 h<br>DON: 8 h (post dosing) < DL<br>DON and de-epoxy DON (conjugated): 12-14 h (post dosing) <20 ng/ml | |
| | | | | → recovery of administered DON: 63%<br>DON (free) 24.1%<br>DON (conjugated) 21.2%<br>De-epoxy DON (free) 0.5%<br>De-epoxy DON (conjugated) 17.2% | |
| | | | Bile | De-epoxy DON (conjugated)<br>$t_{max}$: 0.66-0.75 h (post dosing)<br>5 h (post dosing) = trace levels | |
| Sheep | 4.0 mg [$^{14}$C]-DON/kg BW i.v. | Single dose | Urine | DON and de-epoxy DON (free and conjugated) 91% | Prelusky et al., 1987 |
| | | | Bile | DON and de-epoxy DON (free and conjugated) 6% | |
| | | | | → recovery of administered DON: 3.5% | |
| | | | Urine and bile | → recovery of administered DON:<br>DON (free) 11%<br>DON (conjugated) 67%,<br>De-epoxy DON (conjugated) 13% | |

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TABLE 3 continued

| Animal species | Dose mg/kg diet | Duration day | Deoxynivalenol and its metabolites in serum, urine, bile and duodenal chymus | | Literature |
|---|---|---|---|---|---|
| | | | tissue | concentration and distribution of DON and metabolites | |
| | 880 | 3 | Urine | DON (free): 12 h (post dosing) < DL<br>DON (conjugated): 12 h (post dosing) = 30 ng/ml<br>De-epoxy DON (free): 12 h and 24 h (post dosing) = 130 and 35 ng/ml<br>De-epoxy DON (conjugated): 12 h, 24 h and 48 h (post dosing) = 740, 400 and 98 ng/ml | |
| | 330 | 3 | Urine | DON (free): 12 h (post dosing) = trace levels<br>DON (conjugated): 12 h (post dosing) = trace levels<br>De-epoxy DON (free): 12 h and 24 h (post dosing) = 37 and 15 ng/ml<br>De-epoxy DON (conjugated): 12 h, 24 h and 48 h (post dosing) = 105, 55 and 15 ng/ml | |
| Sheep | 1.0 mg/kg BW i.v. | Single dose | Serum | DON (conjugated): 0.74 min = 345 ng/ml<br><br>→ recovery of administered DON:<br>DON (conjugate) 8 to 15%<br>De-epoxy DON < 1% | Prelusky et al., 1990a |
| Dairy cow | 8.05 and 7.15 mg DON/kg wheat | 35 | Duodenal chyme | → DON and de-epoxy DON flow at the duodenum (% of DON intake): 4-28% | Dänicke et al., 2005 |
| Dairy cow | 4.5 mg/d* (estimated) | Field study | Serum | DON (average) 35 µg/l*<br>Individual values ranged from 8.1 to 58.4 µg/l* | Sabater Vilar, 2003 |

DON = deoxynivalenol; de-epoxy DON = de-epoxy deoxynivalenol; DL = detection limit; p.o. = per oral; i.v. = intravenous; BW = body weight, $C_{max}$ = maximal concentration; $t_{max}$ = time of the maximal concentration, * analyses were performed with ELISA protocols (Biocheck, Leipzig, Germany)

Also, the pharmacokinetics of DON in sheep were investigated. Following a single oral administration of 5 mg/kg BW only a small percentage of 6-10% of the dose was absorbed into the circulatory system as the parent toxin (Prelusky et al., 1985). Conjugated DON of the total plasma DON accounted for 63-86%, with a small fraction present as conjugated de-epoxy DON (1.8-2.8%). Following single intravenous DON administrations of 0.5 mg/kg BW and 1 mg/kg BW only 15-23% and 8-15% of total plasma DON occurred as the DON conjugate, 1.4 to 1.7% and <1% as the de-epoxy DON conjugate, respectively (Prelusky et al., 1985, 1990a). These results suggested that the toxin will go directly to the liver where it can possibly undergo extensive conjugation as a "first-pass effect" when absorbed from the gastrointestinal tract. Glucuronic acid conjugation appears to be an important metabolic pathway, while in comparison, deepoxidation appears to be only a very minor pathway of systemic DON metabolism. Moreover, in subsequent studies DON was administrated intravenous (0.5 mg/kg and 4 mg/kg BW) and was rapidly cleared from the body, essentially excreted in the urine mostly in the form of the glucuronide conjugates (Prelusky et al., 1986, 1987). This suggests that metabolic conjugation of DON appeared to be an important step in its elimination. Furthermore, comparison of systemic elimination of DON and metabolites through urinary and biliary routes suggests that biliary excretion does not play an important role, while urinary excretion appeared to be the most important mechanism (Prelusky et al., 1986).

It is of interest to note that following a large single oral or an intravenous dose of DON, only very little de-epoxy DON (free or conjugated) could be measured in the blood, however a more prolonged oral exposure with a DON contaminated diet for three days resulted in conjugated de-epoxy DON being the major component detected (Prelusky et al., 1987). This appears to be a result of the extended exposure of DON to the rumen microflora, which have the capacity to convert DON to de-epoxy DON. These findings are supported by Dänicke et al. (2004) who fed fistulated dairy cows with *Fusarium* toxin contaminated wheat (8.05 and 7.15 mg DON/kg wheat) over a 35 d period. Only a small fraction of ingested DON of 15% was recovered at the duodenum and the majority (89%) was in the form of de-epoxy DON. Also, the authors suggested a complete degradation of the molecule in the rumen or an absorption by the mucosa of the rumen. Moreover, Prelusky et al. (1985) estimated the systemic bioavailability of DON in sheep at 7.5% on average due in part to its rapid and efficient metabolism by rumen microorganisms. In contrast, adverse results have been obtained by Sabater Vilar (2003). A mean DON content of 32 µg/L was detected in blood serum of dairy cows belonging to a Dutch farm. Based on an average daily intake of 20 kg dry matter, the estimated individual daily DON exposure was 4.5 mg. Sabater Vilar (2003) concluded that these

results clearly indicate a disability of the rumen to degrade the amount of DON to which the animals were exposed. Taking into account that blood samples were analysed by using a DON ELISA these results should be interpreted carefully. Additional investigations on ruminants, especially long term studies with defined experimental conditions, should be performed to evaluate the biotransformation of DON which is essential to evaluate possible carry over into milk.

Carry over of DON and de-epoxy DON to animal products of ruminants is only investigated for transmission in the milk, however no information is available on residues in edible tissues (Table 4). Following a single oral dose of 1.7 mg/kg BW to lactating cows, concentrations of free and conjugated DON in

TABLE 4

Deoxynivalenol (DON) dose and DON and metabolites in milk of ruminants (following Dänicke et al., 2000)

| Animal species | Dose mg/kg diet | Duration Day | Toxins and metabolites in milk, µg/l | Literature |
|---|---|---|---|---|
| Dairy cow | 920 mg p.o. | Single dose | Traces of DON (< 4) (with and without incubation with glucuronidase) | Prelusky et al., 1984 |
| Dairy cow | 50 mg p.o. | Single dose | < 10 | |
| Dairy cow | 66 | 5 | DON < DL, de-epoxide-DON: 2-26 | Cote et al., 1986 |
| Sheep | 880 | 3 | $C_{max}$: DON = 17, de-epoxy-DON = 205 | Prelusky et al., 1987 |
| | 330 | 3 | $C_{max}$: DON = 10, de-epoxy-DON = 125 | |
| Dairy cow | 0, 6, 12 mg/kg concentrate feed | 70 | DON and de-epoxy DON < 1 | Charmley et al., 1993 |

DON = deoxynivalenol; de-epoxy DON = de-epoxy deoxynivalenol; DL = detection limit; p.o. = per oral; $C_{max}$ = maximal concentration

the milk were 1-3 ng/ml at 8 h, and <1-2 ng/ml at 20 h after dosing, respectively (Prelusky et al., 1984). Furthermore, extremely high oral doses of 4.0 and 1.5 g pure DON administered over a 72 h period to sheep resulted in maximum total DON residues of 222 and 135 ng/ml, respectively (Prelusky et al., 1987). Only trace amounts of DON, essentially as conjugated de-epoxy DON could be detected 44-48 h after the last exposure to DON. Cote et al. (1986) detected no unconjugated DON, however concentrations of unconjugated de-epoxy DON ranged up to 26 ng/ml. The authors stress the difference between multiple and single dose administration, but in a study of Charmley et al. (1993) no DON and de-epoxy DON residues were measured in milk from cows when consumed up to 100 mg/d for 70 days.

*Zearalenone*

Kiessling and Petterson (1978) reported on two principal pathways of ZON metabolism in liver homogenate or isolated microsomes of rats using an *in vitro* study: conjugation with glucuronic acid (enzyme glucuronosyltransferase) and reduction to α- or β-ZOL (enzyme 3α (β)-hydroxysteroid dehydrogenase). Investigations on the subcellular distribution of the ZON reducing activity in the liver of cows showed that the NADH- and NADPH-dependent α-ZOL formation were located almost entirely in the microsomal fraction, while β-ZOL formation occurred only in the cytosol fraction with NADPH as coenzyme and no detectable amounts were formed with NADH as coenzyme (Olsen and Kiessling, 1983).

Relatively little information is available about the kinetic behaviour of ZON in ruminants (Table 5). Prelusky et al. (1990b) detected only trace amounts of conjugated ZON declining rapidly to negligible levels following an oral exposure to cows with a ZON contaminated diet (544.5 mg/d) over a period of 21 days or after oral one-day ZON doses of 1.8 and 6.0 g. In another study, Mirocha et al. (1981) found urinary and faecal excretions of free and conjugated (glucuronic and sulphate) ZON of 29 and 25%, α-ZOL of 20 and 12% as well as β-ZOL of 51 and 58% of ZON ingested by cows, whereby the ZON-, α-ZOL- and β-ZOL-glucuronide conjugates of the total urinary ZON accounted for 73.7, 52.9 and 70.0%. These results indicate that the predominant metabolite in urine and faeces was β-ZOL, mainly appearing as glucuronide conjugate. These findings agree with those of Kleinova et al. (2002) who concluded from investigations on heifers which were fed with ZON contaminated oats (1.4 mg/kg) for 84 days that 80% of the ingested ZON analysed as the sum of the parent compound and its metabolites were excreted in urine as α-ZOL and β-ZOL in the ratio 1:8. The concentrations of ZON, α-ZOL and β-ZOL in the liver were distinctly lower than those observed in the urine, the ratio of α-ZOL and β-ZOL was 1:5. Dänicke et al. (2002a) reported on β-ZOL concentrations of 68% of total detected metabolites in bile whereas the respective percentages of α-ZOL and ZON were 8 and 24% due to feeding *Fusarium* contaminated wheat (0.1 mg ZON/kg complete ration) to growing bulls. Similarly, Kennedy et al. (1998) found the ratio between α-ZOL and β-ZOL in the range from 1:2 and 1:3 in bile samples of cattle exposed with naturally ZON contaminated feedstuffs.

With regard to the ban of all hormonal substances used for the purposes of growth promotion of domestic livestock by the European Union in 1988 (Council Directive 88/146), it is important to note that the metabolite α-ZAL, which was used as a growth promoter in beef cattle fattening in the past by commercial preparation of zearalenone marketed under the name Ralgro (International Minerals and Chemical

TABLE 5

Zearalenone (ZON) dose and ZON and metabolites in serum, bile, urine, duodenal chyme and faeces of ruminants

| Animal species | Dose mg/kg diet | Duration day | Zearalenone and metabolites in serum, urine, bile, duodenal chyme and faeces | | Literature |
|---|---|---|---|---|---|
| | | | tissue | concentration and/or distribution of DON and metabolites | |
| Dairy cow | 100 | 7 | Urine | → Distribution of ZON (conjugated and free): ZON 29%, α-ZOL 20%, β-ZOL 51% | Mirocha et al., 1981 |
| | | | Faeces | → Distribution of ZON (conjugated and free): ZON 25%, α-ZOL 12%, β-ZOL 58% | |
| Ewe | 1 mg deuterio-ZON i.v. | Single dose | Urine | ZON, α-ZOL, β-ZOL, α-ZAL and β-ZAL detectable | Miles et al., 1996 |
| | 5mg deuterio-ZON p.o. | Single dose | Urine | ZON, α-ZOL, β-ZOL, α-ZAL and β-ZAL detectable | |
| Cattle | 10 mg ZON | Single dose | Bile | $t_{max}/C_{max}$: ZAL: 96 h (post dosing) = 3 ng/ml<br>$t_{max}/C_{max}$: α-ZOL: 24 h (post dosing)=150 ng/ml | Kennedy et al., 1998 |
| | 10 mg α-ZOL | Single dose | Bile | $t_{max}/C_{max}$: ZAL: 240 h (post dosing)=20 ng/ml<br>$t_{max}/C_{max}$: α-ZOL:12-24 h (post dosing) =200 ng/ml | |
| | 10 mg β-ZOL | Single dose | Bile | ZAL: not detectable<br>$t_{max}/C_{max}$: α-ZOL: 24 h (post dosing)=60 ng/ml | |
| | ZON+α-ZOL + β-ZOL | Single dose | Bile | A-ZOL > ZON > β-ZOL | |
| Dairy cow | 544.5 mg ZON | 21 | Serum | $t_{max}/C_{max}$: ZON (conjugated): 62 h = 3 ng/ml | Prelusky et al., 1990b |
| | 1.8 g ZON | Single dose | Serum | $t_{max}/C_{max}$: ZON (conjugated): 12 h (post dosing) = 9 ng/ml | |
| | 6.0 g ZON | Single dose | Serum | $t_{max}/C_{max}$: ZON (conjugated): 12 h (post dosing) = 13 ng/ml | |
| Heifer | 158 µg/animal | 84 | Urine | ZON and β-ZOL: < 0.5 µg/l | Kleinova et al., 2002 |
| | | | Liver | β-ZOL < 1.0 µg/kg | |
| | 2740 µg/ animal | 84 | Urine | ZON 5-8, α-ZOL 3-5, β-ZOL 20-65, α-ZAL 2-3, β-ZAL < 0.5 µg/l | |
| | | | Liver | ZON and α-ZOL < 0.5 – 1.2, β-ZOL 5-11.5 µg/kg | |
| | 2 x 25 mg α-ZAL pellets + 158 µg/ animal/d | 84 | Urine | ZON and α-ZOL < 0.5, α-ZAL 2-5, β-ZAL < 0.5 µg/l<br>→ 80 % of the analysed ZON in urine and tissue samples was transformed to β-ZOL | |
| Growing bull | 0.1 mg ZON/ kg | 152-160 | Bile | ZON 7-24, α-ZOL 2-11, β-ZOL 23-53 ng/g<br>ZAL < 100, α-ZAL < 50, β-ZAL< 200 ng/g<br>→ β-ZOL, ZON and α-ZOL amounted 68, 24 and 8 % of total metabolites | Dänicke et al., 2002a |
| Dairy cow | 0.76 mg ZON/kg wheat | 35 | Duodenal chyme | → ZON, α-ZOL and β-ZOL flow at the duodenum (% of ZON intake): 43-132 % | Dänicke et al., 2005 |

ZON = zearalenone, α-ZOL = α-zearalenol, β-ZOL = β-zearalenol, ZAL = zearalanone; α-ZAL = zeranol; β-ZAL = taleranol; $C_{max}$ = maximal concentration; $t_{max}$ = time of the maximal concentration

Company, USA), was detected in 6.6% of these samples. The authors suggest that the formation of α-ZAL may occur primarily *via* reduction of α-ZOL, probably in the reductive environment of the rumen. The results are in agreement with earlier investigations which implied that α-ZAL can occur in domestic animals without deliberate α-ZAL treatment (Erasmuson et al., 1994; Kennedy et al., 1995; Miles et al., 1996; Figure 2). Moreover, Kennedy et al. (1998) found significantly higher α-ZOL (12-fold) and β-ZOL (9-fold) concentrations in the α-ZAL positive samples than in the α-ZAL negative samples with an α-ZAL: α-ZOL ratio of at least 1:5. Therefore, the authors suggested using the ratio for a control of the α-ZOL ban, because it is unlikely that an α-ZAL: α-ZOL ratio of less than 1:5 occurs under field conditions. Kleinova et al. (2002) only detected the metabolites α-ZAL, β-ZAL and ZAN in the urine whereas the ratio between α-ZAL or β-ZAL and β-ZOL varied between 1:8 and 1:26. Dänicke et al. (2005), who fed fistulated dairy cows with *Fusarium* toxin contaminated wheat (0.26 and 0.10 mg ZON/kg wheat) over a 35 d period, reported on mean proportions of α-ZOL, β-ZOL and ZON of the sum of these substances at the duodenum of 30, 40 and 30%, however α-ZAL, β-ZAL and ZAN residues were below the detection limits. Moreover, the high recovery of ZON plus metabolites (89%) at the duodenum would imply a rather low complete degradation of ZON in the rumen and/or recovery of some bile-originating enterohepatic-cycling ZON/metabolites (Dänicke et al., 2005).

In addition, ZON and its metabolites have been shown to carry over into ruminant milk (Table 6). Total residues (ZON, α-ZOL and β-ZOL, conjugated and free) of 1.4 mg/l corresponding to 0.7% of the consumed ZON were detected in cow milk after feeding a ZON concentration of 25 mg/kg diet for 7 days (Mirocha et al., 1981). Only 27% of the total metabolites (free and conjugated) occurred as β-ZOL, while 35 and 37% appeared as ZON and α-ZOL. However, Prelusky et al. (1990) found concentrations of total residues mainly containing ZON and α-ZOL conjugates less than 6 µg/kg in milk from a cow that consumed 545 mg ZON/d for 21 days. Also, single ZON administrations of 1800 or 6000 mg given over one day resulted only in trace concentrations of the total residues. Similarly, low traces of ZON and β-ZOL were measured in milk in a study by Hagler et al. (1980) who fed a single dose of 5000 mg ZON to one cow. The capacity of the rumen microorganisms to degrade ZON was discussed as one reason for the widespread discrepancies between the single results of the studies (Prelusky et al., 1990). No residues or only traces were accordingly detected after administration of low ZON doses (Prelusky et al., 1990; Usleber et al., 1992; Goll et al., 1995). Furthermore, only little information is available on ZON residues in edible tissues. In studies by Shreeve et al. (1979) and Dänicke et al. (2002a) residues in muscle, liver, kidney, fat from kidney cavity and back fat were below the detection limits. Also, Kleinova et al. (2002) found no residues in muscle tissues of heifers, which were

TABLE 6
Zearalenone (ZON) dose and ZON and metabolites in milk and edible tissues of ruminants (according to Dänicke et al., 2000)

| Animal species | Dose mg/kg diet | Duration day | Toxins and metabolites in milk and eatable tissues | | Literature |
|---|---|---|---|---|---|
| | | | Tissue | Concentration and/or distribution of DON and metabolites | |
| Dairy cow | 0.39-1.93 mg/ kg concentrate | 49 | Muscle<br>Liver<br>Kidney<br>Milk | ZON < 4 µg/l and µg/kg, respectively | Shreeve et al., 1979 |
| Dairy cow | 5000 mg/animal | Single dose | Milk | ZON and β-ZOL < 1 µg/l (incubation with β-glucuronidase) | Hagler et al., 1980 |
| Sheep | 1800 mg/animal | Single dose | Milk | ZON and β-ZOL 1-2 µg/l (incubation with β-glucuronidase) | Hagler et al., 1980 |
| Dairy cow | 25 | 7 | Milk | 1360 µg/l total-residuals (conjugated and free)<br>→ 0.7% of the ZON recovered in the milk | Mirocha et al., 1981 |
| Dairy cow | 50 and 165 mg/d | 21 | Milk | ZON, α-ZOL and β-ZOL as well as conjugates < 0.5, < 0.5 and < 1.5 µg/l | Prelusky et al., 1990 |
| | 545 mg/d | 21 | Milk | $C_{max}$: ZON and α-ZOL (only as conjugates) 2.5 and 3.0 µg/l | |
| | 1800 and 6000 mg/animal | Single dose | Milk | $C_{max}$: ZON 4.0 and 6.1; α-ZOL 1.5 and 4.0; β-ZOL 4.1 and 6.6 µg/l | |
| Dairy cow | 25 and 100 mg/day | 6 | Milk | $C_{max}$: ZON-equivalent 0.4 and 1.2 µg/l, respectively (determination with Elisa after incubation with β-glucuronidase, particularly detection of α- and β-ZOL) | Usleber et al., 1992 |
| Dairy cow | 0.02 – 0.05 | 63 | Milk | ZON and α-ZOL < 0.5 µg/l | Goll et al., 1995 |
| Heifers | 158 µg/animal | 84 | Liver | β-ZOL < 1 µg/kg | Kleinova et al., 2002 |
| | 2740 µg/animal | 84 | Liver | ZON < 1.0-2.1; α-ZOL < 1.0–2.4; β-ZOL 5.0-11.5 µg/kg | |
| | 2 x 25 mg zeranol pellets+ 158 µg/animal/d | 84 | Liver | No traces of ZAL, α-ZAL, β-ZAL | |
| Growing bull | 0.1 mg/kg | 152-160 | Muscle<br>Liver<br>Kidney<br>Back fat | ZON, α-ZOL, β-ZOL, ZAN, α-ZAL, β-ZAL < 1, < 0.5, < 5, < 100, < 50, < 200 ng/g | Dänicke et al., 2002a |

ZON = zearalenone, α-ZOL = α-zearalenol, β-ZOL = β-zearalenol, ZAL = zearalanone; α-ZAL = zeranol; β-ZAL = taleranol; $C_{max}$ = maximal concentration; $t_{max}$ = time of the maximal concentration

fed with oat diets containing 1370 µg/kg ZON for 84 days. However, in the liver samples of the same animals, β-ZOL (5.0-11.5 µg/kg), α-ZOL (<1.0-2.4 µg/kg) and ZON (<1.0-2.1 µg/kg) could be identified.

## DEOXYNIVALENOL AND ZEARALENONE EFFECTS ON HEALTH AND PERFORMANCE IN DEPENDENCE ON DOSAGE AND DURATION OF TOXIN EXPOSURE

### *Deoxynivalenol*

Noller et al. (1979) fed *Gibberella zeae* infected maize in complete mixed rations to lactating dairy cows and found a slight decrease of daily feed intake with a concomitant decrease of body weight gain, but milk fat and milk production did not differ. The maize offered to the cows was not analysed for DON, however pigs refused the ingestion of this maize-batch. Therefore, the authors supposed the existence of DON in the maize. In agreement with these results, Trenholm et al. (1985) noticed that feed intake was slightly reduced when naturally contaminated grain was added to the ration of non lactating cows. However, no clinical symptoms of illness could be observed that might be attributed to the DON concentration of 1.5 up to 6.4 mg/kg.

Short-term feeding of very high DON concentrations of 66 mg/kg diet during a five day trial affected neither feed intake nor the milk production (Cote et al., 1986). Also, feeding of diets containing DON concentrations of 6 or 12 mg/kg to low-producing dairy cows in a 10 week long-term study did not affect the intake of concentrate or forage (Charmley et al., 1993). It is unlikely that the marked reduction in fat content of the milk and the tendency toward lower fat corrected milk production, when the DON concentration of 6 mg/kg was fed, was caused by the presence of DON, because the effect was not induced by feeding the higher DON concentration of 12 mg/kg. Accordingly, Ingalls et al. (1996) observed no effects on milk performance, milk composition and milk fat amount when feeding DON concentrations up to 14.6 mg/kg concentrate during 21 days. However, Whitlow et al. (1986) found a declined milk production in dairy cow herds when DON concentration in grain increased.

For fattened beef cattle, Schuh (1996) suggested that a chronic exposure with a DON concentration up to 0.5 mg/kg ration would adversely affect performance and cause a decreased feed intake, a lower weight gain and abnormal hair growth. DeHaan et al. (1983) evaluated effects of DON ingestion on feedlot steer, heifer and fattening lamb performance. The authors reported that the presence of DON at a concentration of 1 mg/kg diet given to steers as well as heifers during a 142

day experiment had no deleterious effects on average daily gain, feed intake, feed efficiency and carcass characteristics. Feeding scabby wheat (8.5 mg DON/kg diet) to fattening lambs appeared not to affect feedlot performance. Also, performance data of lambs, which were fed a diet containing DON concentrations of 15.6 mg/kg for 28 days, did not differ from those of the controls (Harvey et al., 1986). In a more extensive study, Nelson et al. (1984) evaluated the effects of a DON contaminated wheat diet (2.3 and 10.0 mg/kg) or a DON contaminated maize-based diet (0.2 mg/kg) on performance, toxicity and pathologic changes in steers and heifers. No adverse effects of DON on tissue histology, serum biochemistry, white blood cell differential count, or glucose, urea, creatinine, calcium, phosphor, sodium and potassium content in blood were observed. Also, DiCostanzo et al. (1995) indicated that feeding dietary DON up to 190.8 mg/d for 135 days did not affect intake, daily gain, feed efficiency and carcass characteristics, serum biochemistry and haematological variables of steers. Comparable results were obtained by recent feeding experiments using feedlot steers consuming dietary DON concentrations up to 221.9 mg/d (Boland et al., 1994; Windels et al., 1995; Dupchak, 1998). In a study of Anderson et al. (1995), who investigated the impact of DON contaminated barley (36.8 mg/kg) fed to yearling heifers during mid and late gestation on pregnancy and birth, no differences in feed intake, cow weight gain or calf birth weight were observed. However, calves nursing cows of the DON contaminated diet during the first 45 days of lactation showed significantly higher gains.

Moreover, numerous studies have been carried out where more than only DON as prevalent toxin in a significant concentration was detected in the feed. Thereby it is difficult to distinguish whether the observed effects are caused by DON alone or by interactions between the toxins. Schuh and Baumgartner (1988) reported diarrhoea in steers fed a diet containing 14.5 mg DON/kg and 4.5 mg T2/kg. Whether this effect was caused by DON, T2 or the interaction is not clear. In another study, Hochsteiner et al. (2000) investigated the effect of naturally DON and ZON contaminated feed on dairy cows. The average daily DON and ZON intake ranged from 12.4 to 14.3 mg and 0.67 to 0.94 mg, respectively. No significant differences could be observed regarding the milk yield and milk ingredients between the different mycotoxin concentrations. Additionally, the enzymes gamma glytamyl transferase and alkalic phosphatase and the metabolites glucose, urea, creatinine and bilirubin in the serum were in the normal range, while slightly increased aspartate aminotransferase and glutamate dehydrogenase activities were determined. In contrast, in an experiment by Dänicke et al. (2002a), who fed growing bulls with *Fusarium* contaminated wheat (10 mg DON and 0.76 mg ZON per kg dry matter), the serum activities of aspartate aminotransferase and glutamate dehydrogenase were unaffected by dietary treatment. However, the

serum cholesterol levels were slightly decreased but the authors noted that this observation is difficult to explain due to the complicated cholesterol metabolism. No explanation could be given for the significantly increased weights of the empty gastrointestinal tract, the significantly decreased empty body weights and the decreased dressing percentages of the slaughtered bulls fed the *Fusarium* toxin contaminated concentrate. With regard to the oestrogenic properties of ZON, weights of the testicles were slightly reduced due to feeding the toxin contaminated concentrate, which possibly indicates an endocrine alteration (Dänicke et al., 2002a).

Furthermore, antimicrobial properties of the mycotoxins, which possibly affect fermentative capacity of the rumen, were observed in *a vitro* study. A decreased volatile fatty acids production and a reduction in gas production were observed with mouldy maize silage in an *in vitro* study using the rumen simulation technique RUSITEC (Maiworm et al., 1995). However, Westlake et al. (1987a, b) tested the influence of the *Fusarium* toxins DON and T2 on the growth of the rumen bacteria *Butyrivibrio fibrisolvens* and observed no inhibitory effect. Rumen physiological investigations including wethers have shown that rumen pH and concentrations of ammonia and volatile fatty acids were not influenced due to feeding a ration of hay and *Fusarium* contaminated wheat (4.6 mg of DON and 0.34 mg ZON per kg of complete ration on dry matter) (Dänicke, 2002b). Also, no impact of feeding DON and ZON contaminated wheat on pH-value and the concentration of volatile fatty acids in rumen fluid of fistulated dairy cows was observed in studies by Dänicke et al. (2005). However, the ruminal ammonia concentration was higher when the contaminated wheat was fed (Dänicke et al., 2005), while the duodenal flow of microbial protein (Dänicke et al., 2005) and of undegraded dietary protein were reduced (Dänicke et al., 2005; Seeling et al., 2005). The authors suggested that the altered ruminal protein utilization could possibly results from the modified chemical and physical properties of the grain caused by the fungal invasion. Higher protease activity, increases in the soluble protein fraction and in the non starch polysaccharide hydrolysing enzyme activities accompanied with significantly reduced cell wall compounds cellulose, xylan and pectin were found in *Fusarium* contaminated wheat (Kang and Buchenauer, 2000; Matthäus et al., 2004; Dänicke et al., 2005).

*Zearalenone*

Mirocha et al. (1968) reported a case study in England where the insemination index increased from 1.2 to 4 when hay of poor quality was fed to a herd of 150 dairy cattle. Analyses of a hay sample resulted in a ZON concentration of 14 mg/kg. The insemination index returned to normal after the hay was replaced. Roine et al. (1971) described a clinical picture with vulva and vagina swelling, abundant mucous discharge from the vulva and false oestrus by dairy cows. *Fusarium graminearum* and *Fusarium culmorum* were isolated from the meal feed and due to their ability to produce considerable amounts of ZON *in vitro,* the authors deduced that the fertility disturbances were caused by ZON. Vulva swelling, reduced milk performance and reduced appetite of dairy cows were observed by Vanyi et al. (1974). The concentration of ZON in the feed amounted up to 75 mg/kg. Furthermore, large doses of ZON were associated with abortions in cattle (Kallela and Ettala, 1984). The presence of ZON at a concentration of 1 mg/kg in a ration of dairy cows was associated with feed refusal, lethargy and anaemia (Mirocha, 1974). In another case report, 2 out of 20 heifers had enlarged mammary glands and the mammary secretion resembled skim milk although the heifers were not pregnant and no oestrus was observed (Bloomquist et al., 1982). The fed maize was covered with a fungal-like growth and a sample was found positive for ZON (no data on concentrations). Epidemiological studies of Schuh (1981, 1983) indicated that ZON contaminated wheat (1.25 mg/kg) fed to dairy cattle led to cystic degeneration of ovaries and to alterations in the consistence of the uterus. Coppock et al. (1990) reported on a herd of dairy cows and replacement heifers which were fed with a ration containing 1.5 mg ZON and 1.0 mg DON/kg. Cows showed frequent episodes of false oestrus of 2 to 5 d duration and idiopathic vaginitis. Furthermore, mammary gland enlargement was observed in the prepubertal heifers. In a study by Möser (2001), heifers were fed with *Fusarium* contaminated ground oats (1.25 mg ZON/kg), while a second group was given a zeranol implant (Ralgro®) twice at intervals of 6 weeks. The animals fed with the contaminated oats showed a higher mean daily weight gain. However, neither any disturbance of the oestrous cycle nor any pathological or histological changes in the reproductive organs were observed due to the influence of ZON and zeranol.

TABLE 7
Effects of the *Fusarium* toxins deoxynivalenol (DON) and zearalenone (ZON) on ruminant performance

| Toxin | Animal species | Experimental description | Symptoms | Literature |
|---|---|---|---|---|
| DON | Dairy cow | Maize was not analysed for DON; however pigs refused ingestion of the maize batch, so that authors supposed the existence of DON in the maize | Slight decrease of daily feed intake<br>No differences in milk fat and milk production | Noller et al., 1979 |
| DON | Heifer<br>Steer | 1 mg/kg diet during 142 days | No differences in animal performance or carcass characteristics | DeHaan et al., 1983 |
| | Fattening lamb | 8.5 mg/kg diet during 45 days | No effect on animal performance | |
| DON | Steer<br>Heifer | 0.2, 2.3 and 10 mg/kg during 126 days | No apparent clinical signs or toxic manifestations<br>No toxicological or pathological changes by serum and whole blood profiles | Nelson et al., 1984 |
| DON | Dairy cow | 1.5 mg/kg during 28 days and 6.4 mg/kg during 70 days | Replacing the lower with the higher DON contaminated feed caused temporary lower feed intakes | Trenholm et al., 1985 |
| DON | Dairy cow | 0 to 0.8 mg/kg concentrate | Milk production decreased when feeding the higher DON contaminated concentrate | Whitlow et al., 1986 |
| DON | Dairy cow | 66 mg/kg during 5 days | No differences in feed intake or milk production | Cote et al., 1986 |
| DON | Lamb | 15.6 mg/kg diet during 28 days | No differences in feed consumption, weight gains or feed efficiency<br>No differences in haematological or serum biochemical variables | Harvey et al., 1986 |
| DON | Dairy cow | 6 mg/kg or 12 mg/kg concentrate during 70 days | No effects on feed intake and milk performance | Charmley et al., 1993 |

Continued on the next page

TABLE 7 Continued

| Toxin | Animal species | Experimental description | Symptoms | Literature |
|---|---|---|---|---|
| DON | Steer | Growing period (84 days): 0.9, 3.7, 6.4, 9.2 mg/kg diet Finishing period (100 days): 1.1, 5.0, 8.8, 12.6 mg/kg diet | No differences for carcass weight, dressing percentage, fat thickness, yield grade and quality grade No differences in feed intake, feed efficiency and weight gain | Boland et al., 1994 |
| DON | Heifer | 36.8 mg/kg barley | No differences in feed intake, weight gain, calf birth weights or blood parameters | Anderson et al., 1995 |
| DON | Steer | 0, 63.6, 127.1 and 190.8 mg/d during 135 days | No effect on feed consumption, live-weight gain and carcass composition | Dicostanzo et al., 1995 |
| DON | Steer | 0, 73.3, 145.2 and 221.9 mg/d during 144 days | No effect on intake, daily gain, feed efficiency and carcass characteristics, serum biochemistry and haematological variables | Windels et al., 1995 |
| DON | Dairy cow | Up to 14.6 mg/kg concentrate during 21 days | No effects on feed intake, milk performance, milk composition and milk fat amount | Ingalls et al., 1996 |
| DON | Steer | 9 to 15 mg/kg ration | No effects on feed intake, weight gain or feed to gain ratio | Dupchak, 1998 |
| DON | Dairy cow | 4.5 mg estimated daily exposure | Decreased red and white blood counts Increased serum activities of GLDH | Sabater Vilar, 2003 |
| ZON | Dairy cow | Determination of ZON (14 mg/kg) in hay | Increased insemination index (1.2 to 4) | Mirocha et al., 1968 |
| ZON | Dairy cow | Determination of *Fusarium graminearum* and *Fusarium culmorum*, which synthesised ZON *in vitro* | Vulva swelling False oestrus Mucus vaginal discharge | Roine et al., 1971 |
| ZON | Dairy cow | 5 up to 75 mg/kg | Vulva swelling Reduced milk performance Reduced appetite | Vanyi et al., 1974 |
| ZON | Dairy cow | 1 mg/kg | Presence of ZON was associated with feed refusal, lethargy and anaemia | Mirocha, 1974 |

Continued on the next page

TABLE 7 Continued

| Toxin | Animal species | Experimental description | Symptoms | Literature |
|---|---|---|---|---|
| ZON | Dairy cow | 1.25 mg/kg | Cystic degeneration of the ovaries<br>Consistence alterations of the uterus | Schuh, 1981, 1983 |
| ZON | Heifer | Determination of ZON in mouldy maize (no data about concentrations) | Bagging up although not pregnant and no oestrus<br>Growth increase<br>Secret similarly milk | Bloomquist et al., 1982 |
| ZON | Ewe | 25 mg purified ZON/d or *Fusarium* culture (contained 25 mg ZON) or<br>Water (controls) during 10 days | Reduced fertility<br>Reduced ovulation rate<br>Longer duration of oestrus | Smith et al., 1986 |
| ZON | Calf | 250 mg purified ZON/d during 3 oestrus cycles | Reduced conception rates (87 to 62 %) | Weaver et al., 1986a |
| ZON | Dairy cow | 500 mg purified ZON/d during 2 oestrus cycles | No effects on progesterone concentration<br>No alteration of genital system | Weaver et al., 1986b |
| ZON<br>DON | Dairy cow<br>Heifers | 1.5 mg ZON/kg feed and 1.0 mg DON/kg feed | False oestrus of 2 to 5 d duration<br>Idiopathic vaginitis<br>Mammary development occurred in the prepubertal heifers | Coppock et al., 1990 |
| ZON | Ewe | 0, 1.5, 3, 6, 12 and 24 mg ZON/day for 10 days starting on day 7 of the oestrus cycle before mating | Decline in ovulation rate<br>Decreased cycle length<br>Increased oestrus duration<br>Reduced incidence of ovulation and fertilization at doses of 12 and 24 mg ZON/d | Smith et al., 1990 |
| | | 0, 1.5, 3, 6, 12 and 24 mg ZON/day for 10 days starting 5 days after mating to entire rams | No effect on pregnancy rate or embryonic loss | |
| ZON | Dairy cow | approximately 0.1 mg/kg feed | Increase in the must secret<br>Changes in behaviour | Drochner, 1990 |
| ZON | Ram | 12 mg ZON/d during 8 weeks | No effects on semen production | Milano et al., 1991 |
| ZON<br>Zeranol | Heifer | 1.25 mg ZON/kg bruised oat or implants:<br>2 applications with 25 mg zeranol at 6 weeks intervals | Animals feeding the contaminated feed showed a higher mean daily weight gain<br>No negative effects on state of health and reproduction tract | Möser, 2001 |

Continued on the next page

TABLE 7 Continued

| Toxin | Animal species | Experimental description | Symptoms | Literature |
|---|---|---|---|---|
| DON<br>T2 | Steer | 14.5 mg DON/kg diet<br>4.5 mg T2/kg diet | Diarrhoea | Schuh and Baumgartner, 1988 |
| DON<br>ZON | Dairy cow | 12.4 mg DON/d and 0.94 mg ZON/d or<br>14.1 mg DON/d and 0.67 mg ZON/d or<br>14.3 mg DON/d and 0.68 mg ZON/d + adsorbents "Mycofix Plus" | No significant differences in milk performance and milk ingredients<br>Increased activities of serum enzymes ASAT and GLDH by all 3 groups | Hochsteiner et al., 2000 |
| DON<br>ZON | Growing bull | 2.2 mg DON and 0.1 mg ZON/kg complete ration with or without adsorbents Mycofix®Plus (Biomin GmbH, Herzogenburg, Austria) | Reduced dressing percentages<br>Increased weight of the emptied gastrointestinal tract<br>Reduced weight of the testicles<br>Slightly decreased cholesterol levels in serum | Dänicke et al., 2002a |
| DON<br>ZON | Wether | 4.6 mg DON and 0.34 mg ZON/kg complete ration with or without adsorbens Mycofix®Plus (Biomin GmbH, Herzogenburg, Austria) | No significant differences in volatile fatty acids and ammonia in rumen fluid<br>Detoxifying agent exert a rumen pH-buffering effect | Dänicke et al., 2002b |
| DON<br>ZON | Dairy cow | 8.05 mg DON/kg and 0.26 mg ZON/kg wheat (35 d)<br>7.15 mg DON/kg and 0.1 mg ZON/kg wheat (35 d) | Higher ammonium concentration in the rumen fluid<br>Reduced crude protein flow, flow of microbial protein and of utilizable crude protein at the duodenum | Dänicke et al., 2005 |
| DON<br>ZON | Dairy cow | 5.2 mg DON and 60 µg ZON/kg concentrate | No significant differences in pH-value in rumen fluid<br>Increase amount of crude protein degraded at the duodenum | Seeling et al., 2005 |

GLDH = glutamate dehydrogenase, ASAT = aspartate aminotransferase

Weaver et al. (1986a) orally administrated a daily dose of 250 mg purified ZON to heifers during one oestrus cycle and for 45 days after they conceived. While the conception rate of the control heifers amounted to 87%, only 62% were observed for the treated group. However, following a daily oral exposure of 500 mg purified ZON during a period of two oestrous cycles, no adverse effects of the progesterone concentration and no alterations of the genital system were found (Weaver et al., 1986b).

Also, the reproductive performance of ewes after administration of ZON was determined (Smith et al., 1986). The exposure of ewes dosed with 25 mg ZON per day for 10 days before mating resulted in prolonged oestrous behaviour, reduced ovulation rate and reduced fertility. Accordingly, daily administration of 1.5, 3, 6, 12 and 24 mg ZON to 33 ewes premating caused a linear decline in the ovulation rate, a decreased cycle length and an increased duration of oestrus (Smith et al., 1990). Reductions in the incidence of ovulation and in fertilization were observed only at daily doses of 12 and 24 mg ZON. There were no effects of ZON treatment (1.5, 3, 6, 12 and 24 mg/d) on pregnancy rate or embryonic loss of the ewes when ZON was administered post mating. Apparently, ewes are only influenced by ZON when dosed prior to mating. In contrast, adult male sheep seemed to be unaffected by ZON administration. In a study by Milano et al. (1991) rams were fed a diet of naturally contaminated maize containing 12 mg ZON/kg (equivalent to 12 mg ZON/d) for eight weeks. No significant effects of sperm production, spermatozoal mass motility and spermatozoal morphology were observed.

## FACTORS OTHER THAN DOSAGE AND DURATION OF TOXIN EXPOSITION WHICH COULD INFLUENCE THE VARIABILITY OF TOXIN EFFECTS IN RUMINANTS AND OF CARRY OVER

### *Species and race*

With regard to the mycotoxins DON and ZON it has been well documented that wide differences exist in sensitivities between several animal species which are also reflected in the orientation values for critical concentrations of DON and ZON in feedstuffs (BML, 2000; Table 8). Monogastric animals, especially pigs, show the greatest sensitivity, while chickens and ruminants appear to have a higher tolerance. The higher insensitivity of ruminants to the toxins is attributed to the metabolization of these substances by microbes in the rumen. Several *in vitro* studies have demonstrated that DON undergoes rapid biotransformation to de-epoxy DON by rumen microflora before being absorbed. Results of Kiessling et al. (1984), who were unable to show any degradation of DON by rumen

TABLE 8
Orientation values for critical concentrations of deoxynivalenol and zearalenone in the diets for pigs, ruminants and gallinaceous poultry, mg/kg at 88% dry matter (BML, 2000)

| | Animal species | Deoxynivalenol | Zearalenone |
|---|---|---|---|
| Pig | Prepubertal female breeding pigs | 1.0 | 0.05 |
| | Fattening pigs and breeding sows | 1.0 | 0.25 |
| Poultry | Laying hens and fattening hens | 5.0 | -[1] |
| Cattle | Calves (preruminating) | 2.0 | 0.25 |
| | Female rearing cattle/dairy cows | 5.0 | 0.5 |
| | Fattening cattle | 5.0 | -[1] |

[1] no orientation values are required at the present time

ingesta *in vitro,* are in contradiction with the findings of other authors. King et al. (1984) demonstrated that DON was almost completely metabolized to a single deepoxidation product within 24 h using bovine rumen fluid, while Ivie (1976) showed an epoxide to olefin transformation by rumen digesta. In a study by Swanson et al. (1987) incubation periods longer than 48 h are required for complete biotransformation of DON to de-epoxy DON. Also He et al. (1992) detected the de-epoxy metabolite of DON after anaerobe incubation of rumen fluid. Although the protozoa fraction seems to be more effective in toxin degradation than the bacterial fraction, the rumen bacteria appear to have increased resistance to the toxic effects of trichothecenes (Westlake et al., 1989). Whitlow and Hagler (1999) noted that, although not compared directly up to now, beef cattle and sheep appear to be less sensitive to DON than dairy cattle. The authors supposed that differences could be related to level of production stress, since mid-lactation, low-producing dairy cattle also appear to be more tolerant to DON than high-producing dairy cattle in early lactation. Early lactating, high producing cows experience greater stress, lower immunity, marginal nutrient deficiencies and a faster rumen turnover and it is possible that these factors are responsible for the higher vulnerability.

Also, several *in vitro* studies with bovine rumen fluid indicate that ZON was almost completely degraded to α- and β-ZOL after 3 up to 10 h, whereby the amount of degradation was dependent on the concentration of ZON (Kallela and Vasenius, 1982; Kiessling et al., 1984; Miettinen and Oranen, 1994). β-ZOL was particularly metabolized to α-ZOL and the parent toxin, while α-ZOL was regenerated only to a minor extent to ZON (Lerch, 1990). Also, *in vitro* investigations of Valenta and Vemmer (1996) confirmed the formation of ZON to α- and β-ZOL at the ratio 2:1 and 3:1, but approximately 50% of the added ZON remained after 24 h. Moreover, ZON as well as the isomers zearalenol could be detected after incubation of α- and β-ZOL. The authors assumed that

a redox equilibrium between ZON and the two metabolites exists and therefore a complete degradation of ZON to α- and β-ZOL in the rumen seems to be questionable. Moreover, Kallela and Vasenius (1982) supposed that the higher tolerance of ruminants to ZON can be attributed to the ruminal metabolization of the toxin. However, the transformation of ZON to α- and β-ZOL is not regarded as detoxification because both products are still oestrogenic (Hagler et al., 1980; see chapter Zearalenone). Therefore, other factors may have caused the lesser toxicity of ZON to ruminants. Possibly, differences in response to ZON are related to differences in the affinity of ZON and its metabolites to the oestrogen receptor since Fitzpatrick et al. (1989) showed that considerable differences in the affinity of α-ZOL to the oestrogen receptor exist between pigs, rats and chickens.

*Age*

Bauer (2002) suggested that preruminating calves are similarly sensitive to mycotoxins as monogastric animals. As mentioned above, ruminants are generally less susceptible to *Fusarium* toxins as compared to monogastric animals which is related to the metabolization of these substances by microorganisms in the rumen. However, with regard to the rumen development, differences should be considered between fattening cattle, dairy cows, ruminant and preruminant young calves. In a study with calves and ochratoxin A, a mycotoxin produced by the fungal genera *Aspergillus* and *Penicillium*, Sreemannarayana et al. (1988) suggested that age as a determinant in the development of a functional rumen greatly modifies the susceptibility of young calves to the toxic action of the toxin. *In vitro* studies with rumen fluid collected from cows and sheep showed that ochratoxin A is hydrolysed enzymatically by microflora in the rumen to the non-toxic dihydroxyisocoumarin (ochratoxin α) by splitting-off the amino acid phenylalanine which is responsible for toxicity (Kiessling et al., 1984; Xiao et al., 1991). Sreemannarayana et al. (1988) administered an oral dose of ochratoxin A of 4.0 mg/kg BW to two preruminant calves. Both calves died within 24 h. At a lower oral dose of 1 mg/kg BW administered to two preruminant calves, one calf died 12 h after dosing, the second survived for 10 days. In contrast, all four calves with functional rumen receiving orally 2.0 mg ochratoxin A/kg body weight survived without overt ill effects. These results confirm that the capacity of detoxification also depends on development of the rumen which becomes functional at 4 to 6 month (Ribelin, 1978). This can explain the higher tolerance of ruminant calves to harmful or toxic substances such as DON in comparison to preruminant calves.

Age and sex dependent differences in the susceptibility to ZON are also known for pigs. Especially prepubertal female pigs react most sensitively which is attributable to their available oestrogen receptor affinity as well as the lack of

competition of own oestrogens, while sows are more tolerant due to their high cyclic oestrogen levels (Drochner, 2002). Likewise, female ruminants show increased oestrogen concentrations in the blood with progressing pregnancy. Therefore, it is possible that the natural differences in the oestrogen level are also responsible for varying sensibilities of female calves, heifers, and low- and high-producing dairy cows to ZON.

*Ration composition*

While *in vitro* experiments of Valenta and Vemmer (1996) did not show an obvious influence of the feeding regime on the metabolization of ZON to α-ZOL and β-ZOL, Kallela and Vasenius (1982) indicated that the quality of rumen fluid had a significant effect on the ratio of the toxin metabolization. This assumption is consistent with results of several *in vitro* studies with ochratoxin A (Müller et al., 1998, 2001; Özpinar et al., 1999). Müller et al. (2001) added pure ochratoxin A to rumen fluid from cows which were fed six diets containing grass, grass silage or hay and two different amounts of concentrate consisting of barley and soyabean meal. The authors observed a disappearance of ochratoxin A accompanied by an appearance of ochratoxin α in the rumen fluid by replacing grass silage or hay by fresh grass and by increasing the level of concentrate in the total diet. They concluded that the decrease of ochratoxin A resulted from an increased number and/or activity of protozoa which are able to hydrolyse the toxin and which are known to increase in total numbers when level of concentrate and thereby amount of metabolizable energy is increased (Eadie et al., 1970; Abe et al., 1973). Accordingly, Özpinar et al. (1999) found an increased velocity of degradation of ochratoxin A in ruminal fluid when the concentration of starch in the diet increased, while an influence of the pH-value was not apparent. However, Xiao et al. (1991) observed a five-fold lower rate of ochratoxin A metabolization to ochratoxin α by using ruminal fluid with a lower pH. Accordingly, He et al. (1992) reported that the response of chicken large intestine contents dosed with DON was also pH-dependent. The biotransformation of DON was inhibited when pH of the media was decreased. A lower ruminal pH is well known to be a result of a higher concentrate level in the feed, and especially fattening ruminants and high-yielding dairy cows are fed diets containing higher amounts of concentrate and lower amounts of roughage. Furthermore, in consideration of the small amount of crude fibre in such diets, Lew (1999) supposed a not completely functional rumen with a lower detoxification capacity. Therefore it is possible that high performing ruminants, which are fed diets containing high levels of concentrate, can already show clinical effects when DON containing diets with concentrations as low as 0.5 mg/kg are fed over longer periods of time (Schuh, 1996).

It can be concluded that the diet of ruminant animals, which can affect rumen microbial composition and numbers (Mackie et al., 1978; Leedle et al., 1982), may be an important determinant in the relative toxin resistance of these animals (Westlake et al., 1989).

*Passage rate*

The essential digestibility processes of ruminants are dependent on microbial fermentation. As explained in chapter Species and race, the mycotoxins DON and ZON are also metabolized by rumen microorganisms. Therefore it is possible that factors affecting the digestibility of dietary components could also influence the metabolization of the toxins.

Faichney (1980) suggested that the extent of digestibility of dietary components in the rumen is a function of rate of digestion and rate of passage. The latter, in turn, is also affected by the level of feed intake. A decreased level of feed intake is associated with a decreased rate of passage (Evans, 1981; Uden, 1984), whereas a high passage rate is related to a lower ruminal retention time. Ruminal retention time of dietary ingredients is quite variable and varies not only from one diet to another, but also between animals and species (Tamminga, 1979). Rumen retention times are higher in beef animals than in dairy cows and they also differ between dairy cattle because level of feed intake varies up to five-fold or more during the course of lactation (Sniffen and Robinson, 1987; Tarr, 1996). It is possible that the retention time of the feed in the rumen, as result of the feed intake, could affect the ruminal metabolization of the toxins. A rapid passage rate may limit the metabolization of the mycotoxins in the rumen. Therefore, it is possible that due to a passage rate dependent metabolization, the toxin and metabolite profile could be altered which could modify the toxicity. However, regarding the *Fusarium* toxins DON and ZON, no data are available of studies which consider feeding situations resulting in different ruminal passage rates.

## CONCLUSIONS

This review has shown that it is difficult to draw conclusions for the practical feeding of DON and ZON contaminated feedstuffs to ruminants due to the limited and inconsistent literature data on the effects of the toxins on health and performance of these animals. Moreover, very little information is available about factors others than time of exposure and dose of the toxins, which could influence the variability not only of toxin effects but also of carry over of these toxins and/or their metabolites into milk and other foodstuffs of ruminant origin.

In most instances merely case or field reports were given. Experiments under controlled conditions were only performed with rather low numbers of animals during limited periods of time using either purified toxins or naturally contaminated feed, which can contain a natural cocktail of several mycotoxins. Then it is often not possible to distinguish whether mycotoxicosis results from the exposure of one mycotoxin or of a group of other not detected/unknown toxins/ substances, the interactions between the different toxins/substances or maybe from fungus related modifications of the feed.

Therefore, accurately defined studies with ruminants, especially with lactating dairy cows, feed DON and ZON in practically relevant concentrations during a longer period are required. In addition, future research should consider genetic and physiological factors such as age, hormone status, nutrition and ruminal microflora which also seem to influence the variability of the effects of DON and ZON on the health of ruminants and on carry over.

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STRESZCZENIE

**Znacznie toksyn *Fusarium*, deoxynivalenolu i zearalenonu, w żywieniu przeżuwaczy**

Deoxydivalenol (DON) i zearalenon (ZON), wytwarzane przez gatunki *Fusarium,* są mykotoksynami odgrywającymi znaczącą rolę w rolnictwie ze względu na ich wpływ na zdrowie zwierząt. ZON powoduje u zwierząt syndrom estrogeniczny, a umiarkowane dawki DON powodują zmniejszenie wydajności i odporności u zwierząt. Spośród zwierząt gospodarskich przeżuwacze lepiej tolerują oddziaływanie DON i ZON, a w konsekwencji producenci pasz dla przeżuwaczy mogą używać w produkcji mieszanek zboża i pasze objętościowe porażone toksynami *Fusarium*. W związku z intensywnym występowaniem toksyn w tzw. latach *Fusarium* możliwość ich wpływu na przeżuwacze nie może być pominięta. W literaturze można spotkać tylko nieliczne i sprzeczne dane dotyczące wpływu DON i ZON na przeżuwacze. W niniejszym opracowaniu przeglądowym omówiono kinetykę, biotransformację, efekt przenośny oraz oddziaływanie DON i ZON u przeżuwaczy. Rozważono i przedyskutowano również wielkość dawek i czas oddziaływania toksyn, jak też czynniki genetyczne i fizjologiczne i ich wpływ na zmienność reagowania przeżuwaczy na toksyczne działanie tych mykotoksyn. W podsumowaniu stwierdzono, że konieczne są dalsze badania nad wpływem DON i ZON na organizm przeżuwacza, szczególnie krów dojnych.