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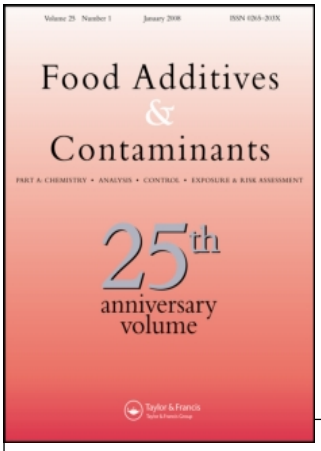

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Mycotoxins in cattle feeds and carry-over to dairy milk: A review

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Mycotoxins in cattle feeds and carry-over to dairy milk: A review

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Abstract
The complex diet of ruminants, consisting of forages, concentrates, and preserved feeds, can be a source of very diverse mycotoxins that contaminate individual feed components. A number of mycotoxins are successfully inactivated by the rumen flora, whereas others pass unchanged or are converted into metabolites that retain biological activity. Hence, the barrier function of the rumen largely determines the susceptibility of dairy cows and other ruminant species towards individual mycotoxins. An impairment of this barrier function due to diseases or the direct antimicrobial effect of certain mycotoxins may increase absorption rates. The rate of absorption determines not only the internal dose and risk for adverse health effects, but also the excretion of mycotoxins and the biologically active metabolites into milk.

Keywords: *Mycotoxins, ruminants, dairy cows, aflatoxins, ergot alkaloids, carry over, milk, biological barriers*

Introduction

The contamination of feedstuffs with mycotoxins is of increasing concern as changes in agricultural practice and probably climatic changes seem to have increased the prevalence of mycotoxin contamination. Contamination of feeds with mycotoxins accounts for significant economic losses in animal husbandry, as well as in undesirable trade barriers for raw materials and consumable products (Wu 2006). Experimental data and clinical experience suggest that ruminants are less susceptible than other animal species to the adverse health effects associated with mycotoxin exposure. This assumption is based on the finding that the forestomach (rumen) flora can convert a number of mycotoxins into metabolites that are less potent or even biologically inactive at common exposure levels. This does not apply, however, to all mycotoxins that contaminate feed materials.

It is the aim of this brief review to identify and describe the uncertainties in the assessment of mycotoxins in the diet of dairy cows in terms of exposure assessment with reference to the physiological and pathophysiological parameters that modulate mycotoxin exposure. Moreover, the mechanisms involved in the excretion of mycotoxins with milk, and potential risk factors associated with the transfer to milk are reviewed.

Mycotoxins in feeds for dairy cattle

In professional animal operations, monogastric species such as pigs, poultry, and fish receive a standardized diet designed to meet the nutritional requirements of the species and age group. The components used in the production of these mixed feeds can be monitored and allow the formulation of diets that are well tolerated by the animals. In contrast, the unique physiology of ruminant species, which is characterized by a pre-systemic fermentation and digestion of plant constituents such as cellulose by microbes comprising the ruminal flora, requires feeding regimes that include sufficient amounts of roughage to maintain a functional rumen flora.

Genetic selection for high milk yield made it necessary to add increasing quantities of digestible

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energy-rich feed components to the ruminant diet. In extensive farming, grazing makes up a large portion of the diet and the intake of concentrates is limited to a few per cent of the total feed intake. In contrast, in dairy cattle operation, concentrates may feature up to 70% of the daily feed ration. A direct consequence of the complex and variable composition of ruminant diets is the risk of exposure to more than one mycotoxins or mycotoxin cluster; the term 'cluster' refers to a set of mycotoxins produced by an individual fungal species (Table I).

The first identified source of mycotoxins in ruminant diets was the contamination of concentrates with aflatoxins. Aflatoxins occur in many typical energy-rich concentrates as, for example, cereal grains, corn gluten, soybean products, as well as in press cakes from oil plants such as peanuts, sunflower seeds, cotton seeds, palm kernels, and copra. Other prominent mycotoxins, such as fumonisins and zearalenone, occur in maize (and maize derived products), whereas cereal grains are contaminated frequently with trichothecenes, particularly with deoxynivalenol, ochratoxins, and ergot alkaloids (Nawaz et al. 1997; Scudamore, Nawaz, Hetmanski 1998; Scudamore, Nawaz, Hetmanski, Rainbird 1998; Placinta et al. 1999).

At the same time, ruminants might be exposed to entirely different classes of mycotoxins that occur in forages (pasture grasses), such as the *Neotyphodium* toxins of the lolitrem-paxilline group and ergovaline, as well as other ergot alkaloids. The level of contamination of (cold season) grasses shows significant geographical differences (Cheeke 1995) and is gaining increasing attention.

The third source of mycotoxins in the diet of dairy cows results from the consumption of preserved feeding stuffs such as silage, hay, and straw (O'Brien et al. 2005; Mansfield and Kuldau 2007). Particularly after a longer storage period, silage can be spoiled by a variety of fungal species, which are acid-tolerant and micro-aerobe. Mycological investigation identified *Penicillium* spp. such as *P. roqueforti* and *P. paneum*, *Aspergilli* (*A. fumigatus* and *A. flavus*) (Cole et al. 1977), *Monascus* spp. (Schneweis et al. 2001), and *Byssochlamys nivea* (Escoula 1975) as the most prevalent fungal species in silage. Mycotoxins produced by these fungi include patulin, mycophenolic acid, penicillic acid, roquefortins, marcfortine A, andrastin A, gliotoxin, and toxins of the verruculogen/fumitremorgen group (Garon et al. 2006; O'Brien et al. 2006). It should be mentioned that mycotoxins originating from pre-harvest contamination of forages that are ensiled are often unaffected by the ensiling process, and add to the overall mycotoxin contamination.

The ratio in which these different feed sources are used in the diet of dairy cows varies considerably and is determined by regional differences, the production stage of the animal, and farm management. This also implies that a generally applicable exposure assessment is not feasible, and hence data relating exposure to multiple toxins to quantifiable markers of animal health and productivity are scarce.

Table I. Examples of possible co-exposure of dairy cows to mycotoxins in different components of a ruminant diet.

Diet component	Mycotoxins
Concentrates	aflatoxins, fumonisins, zearalenone, trichothecenes (DON), ergot alkaloids
Pasture grasses	lolitrems, paspalitrems, penitrem A, ergovaline and associated ergot alkaloids, trichothecenes
Preserved feeds (silage)	patulin, mycophenolic acid, roquefortines, fumitremorgens, verruculogen, monacolines, and others

Clinical mycotoxicoses in dairy cows

Typical clinical intoxications that are well described in ruminants are fescue toxicosis and staggers (reviewed by Fink-Gremmels 2005). Both disease complexes are related to pasture grasses that are infected with endophytes. Tall fescue (*Festuca arundinacea*) is a major forage grass in North America, and infection with the endophyte *Neotyphodium coenophialum* is associated with the production of various alkaloids, the most prominent of which is ergovaline. Cattle exposed to contaminated forages or hay develops a heat intolerance characterized by malign hyperthermia, and peripheral gangrene (fescue foot), reflecting the vasocontrictive properties of ergot alkaloids. In addition, ergovaline acts as a dopamine-receptor agonist, causing a reduced milk yield and lower conception rates (Browning 2000). Recent data show that following ingestion of ergovaline-contaminated tall fescue straw, not only ergovaline, but also lysergic acid is detectable in the urine and faeces of exposed cattle. A mass-balance study revealed that the toxin concentration in ruminal fluid apparently increases over time (De Lorme et al. 2007). These unexpected findings resulted in the hypothesis that the rumen fermentation processes can liberate non-extractable toxins (escaping the initial feed analysis) and metabolize ergovaline into lysergic acid that might be even be absorbed through the ruminal wall (Hill et al. 2001). Although, certainly, further investigations are necessary to support these assumptions, the data clearly indicate that the rumen metabolism does not necessarily result in toxin inactivation. At the same

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time, these data also demonstrate the uncertainties in correlating in-feed concentrations of mycotoxins to the internal dose and to predictable biological effects.

The staggers syndrome observed in cattle and sheep, and also horses, is associated with the exposure to lolitrems and probably paxilline. Perennial ryegrass (*Lolium perenne*) harbours the endophyte *Neotyphodium lolii*, and for many years outbreaks of intoxication were only reported in Australia and New Zealand. However, already in the 1990s, clinical intoxications were reported from North and South America as well as from Europe (Fink-Gremmels 2005, and references therein). Typical clinical symptoms are muscle fasciculation, tremor, and ataxia, which might even progress into tonic convulsions. As probable mechanisms of action, the impairment of the GABAergic pathways (Smith et al. 1997; Wang et al. 2003), was recently challenged by the finding that lolitrem has a potent effect on potassium channel conductance (Dalziel et al. 2005). *Neothyphodium lolii* produces not only tremorgenic toxins, but also peramine, which exerts a potent repellent effect that protects infected plants from insect plagues and earthworm damage, exemplifying the unique symbiosis between endophytes and their hosts.

In addition to these typical mycotoxicoses, the potential adverse effects of other mycotoxins are less well documented in dairy cows. Various reports describe a reduced feed consumption and other adverse health effects associated with the consumption of mouldy feed (hay, silage), and feed materials contaminated with mycotoxins (Osweiler 2000; Hussein and Brasel 2001; Puntenny et al. 2003). A critical analysis of the individual reports indicates, however, obvious gaps in many of the individual case descriptions, as often essential data, such as the amount of feed consumed per day, the animal's body weight, the time of exposure, the presence of other contaminants in the diet, and the animal health status, are not reported. This also applies to the reported outbreaks of acute mycotoxicoses such as *Aspergillus clavatus* toxicosis (Sabater-Vilar et al. 2004), pithomycotoxicosis, which is only incidentally observed in Europe (Pinto et al. 2005), and *Diploida maydis* toxicosis (Odrizola et al. 2005).

Conversion of mycotoxins by the rumen flora

Kiessling et al. already stated in 1984 that ruminating animals are developing mycotoxicoses less frequently as the rumen flora acts as a first line of defence against mycotoxins (Kiessling et al. 1984). For example, ochratoxin A is rapidly converted into the less toxic ochratoxin α (lacking the phenylalanine moiety) by the forestomach flora, and only very small amounts of intact ochratoxin A are absorbed. *In vitro* studies showed that ochratoxin A is mainly degraded by rumen protozoae, and that in healthy cattle up to 12 mg of ochratoxin A per kg feed could be inactivated. This effective deactivation explains the high comparable high tolerance of ruminants to ochratoxin A exposure (Hult et al. 1976; Pettersson et al. 1982). Drastic changes in the feed composition, and a high percentage of protein-rich concentrates in the daily diet modify, however, the cleavage capacity of rumen microorganisms (Xiao et al. 1991; Muller et al. 2001), which explains why incidentally small amounts of ochratoxin A could be detected in milk (Skaug 1999).

The susceptibility of ruminants to deoxynivalenol (DON) is low, as DON is converted almost completely into the less toxic DOM (the de-epoxidized metabolite of DON) by the rumen flora. Studies by Ingalls (1996) showed that ruminating cattle may tolerate diets containing up to 8.5 mg g^{-1} DON for several weeks without major health effects. In a recent study, dietary DON concentrations ranging between 3.1 and 3.5 mg g^{-1} feed (88% DM) did not cause any significant adverse health effects, but transiently increased post-prandial ammonia concentrations (Dänicke et al. 2005; Seeling, Boghun 2006; Seeling, Dänicke, et al. 2006).

Aflatoxins are only partly degraded by the ruminal flora, and a typical secondary metabolite of rumen metabolism is aflatoxicol. Exposure to aflatoxins results in an impairment of liver function and reduced feed intake, which might also explain the reduced milk production in dairy cattle exposed to aflatoxins. The impairment of hepatic functions might also account for the photosensitization associated with aflatoxin exposure (Miller and Wilson 1994).

Zearalenone is converted by the rumen flora into its hydroxy-metabolite α-zearalenol (approximately 90%) and to a lesser extend to β-zearalenol (Kiessling et al. 1984; Kennedy et al. 1998). Although α-zearalenol has a higher oestrogenic potency compared with the parent zearalenone, its lower rate of absorption and its interconversion in the liver to the less potent β-zearalenol might account for the low susceptibility of dairy cattle (Diekman and Green 1992; Dänicke et al. 2005; Seeling et al. 2005). Zearalenone and its metabolites can be excreted with milk, but levels are very low often remaining below the limit of quantification (Seeling et al. 2005).

Fumonisins pass the rumen, and an intake of 3 mg fumonisin B_1 kg^{-1} body weight day^{-1} by Jersey cows for 14 days led to a decreased feed intake and milk production (Richard et al. 1996; Caloni et al. 2000). Signs of intoxication also included an elevated serum enzyme activity of diagnostic liver enzymes (aspartate aminotransferase (AST) and

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gamma-glutamyl-transferase (GGT)), suggesting mild hepatocellular injury. Feeder calves showed signs of immunotoxicity in the form of a significantly reduced lymphoblastogenesis (Osweiler et al. 1993). These effects were observed at feed concentrations that corresponded to exposure rates varying between 2.4 and 3.5 mg g^{-1} body weight.

Mould contamination might also change the digestibility of individual feed components. Seeling, Dänicke, et al. (2006) describe, for example, an increased crude protein degradation and a lower molar percentage of propionate in the rumen when *Fusarium*-contaminated wheat was fed to dairy cows. Certain mycotoxins such as, for example, patulin affect the rumen fermentation (Morgavi et al. 2003) and decrease acetic acid production and protein synthesis (Escoula 1992).

Taken together, these examples demonstrate the correlation between the capacity of the rumen to inactivate mycotoxins and the likelihood of adverse health effects in cattle. At the same time, it becomes evident that for many toxins that can be expected in the diet of dairy cows the rumen stability and the oral bioavailability have not yet been investigated. In addition, the increasing use of protected concentrated (proteins) that are designed to bypass the rumen might influence the oral bioavailability of mycotoxins.

Feed-to-milk transmission of aflatoxins in dairy cows as an example of intra-species variability related to different feeding regimes

Aflatoxins are the most intensively studied mycotoxins in dairy cattle as the excretion of aflatoxin M_1 in dairy milk is of public health concern. Following ingestion of aflatoxin-contaminated feeds, a part of the ingested aflatoxin B_1 is degraded in the rumen, resulting in the formation of aflatoxicol. The remaining fraction is absorbed in the digestive tract by passive diffusion and is hydroxylated in the liver to aflatoxin M_1 (Kuilman et al. 2000). Aflatoxin M_1 is either conjugated to glucuronic acid, and subsequently excreted via bile, or enters the systemic circulation. Circulating aflatoxin M_1 can be excreted in the urine or appear in milk.

Initially, the excreted amount of aflatoxin M_1 in milk of dairy cows was estimated to represent 1–2% of the ingested aflatoxin B_1 (for a review, see Van Egmond 1989). The extent of transfer from feed to milk (carry-over) is influenced by various nutritional and physiological factors, including feeding regimens, rate of ingestion, rate of digestion, health of the animal, hepatic biotransformation capacity, and actual milk production. This implies that the rate of absorption of aflatoxins, and the excretion of aflatoxin M_1 in milk, varies between individual animals, from day to day, and from one milking to the next. In high-yielding cows, the consumption of significantly higher amounts of concentrated feeds might result in carry-over percentages as high as 6.2% (Veldman et al. 1992).

The carcinogenic potency of aflatoxin M_1 is almost as high as that of aflatoxin B_1, and the toxicological properties are generally comparable (Henry et al. 2001). In consideration of these toxicological findings, many countries have set maximum acceptable levels for aflatoxin M_1 in milk and dairy products. Following the risk evaluation by the Joint Expert Committee on Food Additives (JECFA) *Codex Alimentarius*, regulatory bodies in many countries, including the US Food and Drug Administration (USFDA) set a maximum permissible level for aflatoxin M_1 in milk of 0.5 μg Kg^{-1}. In contrast, in Europe, as well as some countries in Africa, Asia and Latin America, the maximum acceptable level is set at 0.05 μg aflatoxin M_1 kg^{-1} milk, with reference to the relative high consumption of milk and dairy products by children (reviewed by Van Egmond et al. 2007). To achieve this objective, statutory limits were defined for animal feeds, including feeds for dairy cows.

Subsequently, several authors have tried to determine whether the current legislation on aflatoxin B_1 in feed (2002/32/EC (OJL 140, 30.05.2002)) for lactating animals is sufficient to keep aflatoxin M_1 levels in milk below the threshold of 0.05 μg Kg^{-1}. Pettersson has already established a model calculation to determine the carry-over of ingested aflatoxin B_1 to aflatoxin M_1 in milk (Pettersson 1998). This equation was based on ten observations from five controlled experiments, and is expressed as follows ($r^2 = 0.915$):

$$\text{Aflatoxin } M_1 \text{ (ng kg}^{-1}\text{ milk)} = 10.95 + 0.787 \times (\mu\text{g aflatoxin } B_1 \text{ intake day}^{-1}).$$

However, a data analysis performed in 2004 on all trials in which daily feeding contained less than 150 μg aflatoxin B_1 kg^{-1} feed (21 observations from six individual studies) yielded a lower regression coefficient ($r^2 = 0.417$), pointing towards a larger margin of uncertainty. In addition, a model calculation for a worst-case scenario of aflatoxin carry-over into milk was performed for the major milk-producing animal species, including dairy cattle, sheep, goats, camels, and buffaloes, and included carry-over rates of 2% (assumed average) and 6% (high yielding cows) (European Food Safety Authority (EFSA) 2004). This model calculation indicated that in a worst-case situation, aflatoxin M_1 levels in milk might exceed the maximum acceptable level of 0.05 μg kg^{-1}, set by the European Union, even if

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the given feed materials comply with the current feed legislation. This might occur in all the mentioned animal species.

As yet, aflatoxin M_1 has been considered to be the major metabolite excreted with milk in dairy cows and other ruminants. In addition, aflatoxin M_2 and M_4, originating from hepatic-biotransformation reactions of other natural aflatoxins, have been found to be excreted with milk, albeit at very low amounts. However, recent data show that aflatoxicol is also excreted with milk (Carvajal et al. 2003). As mentioned above, aflatoxicol is the major metabolite of aflatoxin B_1 produced by microorganisms of the rumen flora. This could be elegantly demonstrated in *in vitro* studies using radiolabelled aflatoxin B_1 (Auerbach et al. 1998). Studies with isolated functional bovine hepatocytes, however, failed to show any formation of aflatoxicol, excluding that hepatic biotransformation contributes to aflatoxicol tissue levels (Kuilman et al. 2000). The carcinogenicity of aflatoxicol has been investigated only in the rainbow trout, an experimental animal model known to be very sensitive to the hepato-carcinogenicity of aflatoxin B_1. Results demonstrated that the carcinogenic potency of aflatoxicol is comparable with that of aflatoxin B_1, and that it is even more potent than aflatoxin M_1 in this model (Hendricks et al. 1980; Schoenhard et al. 1981; Hendricks 1994). A recent study in Mexico, conducted between 1996 and 1998, measured aflatoxicol levels in 580 samples of (ultra) pasteurized milk from different regions in Mexico (Carvajal et al. 2003). Aflatoxicol was present in 13% of the samples at concentrations of $\geq 0.05\,\mu g\,l^{-1}$ and in 8% of the samples at $\geq 0.5\,\mu g\,l^{-1}$, and levels were not influenced by pasteurization. These results need to be confirmed as they suggest a need to monitor the occurrence of aflatoxicol in milk and dairy products. The likely reason why aflatoxicol has not been described earlier in milk is the lack of fluorescence of aflatoxicol, while aflatoxin M_1, M_2 and M_4 retain the fluorescence spectrum typical for aflatoxins. The lack of fluorescence requires detection methods that are different from those commonly used of aflatoxin M_1.

Feed-to-milk transmission of other mycotoxins and factors affecting transmission rates

As yet, aflatoxin M_1 is the only mycotoxins for which maximum permissible levels in milk have been established. However, considering the wide range of mycotoxins that might occur in ruminant diets, the number of available studies addressing the transfer of mycotoxins into milk is very limited. Table II provides a summary of the available data (for detailed

Table II. Products of ruminal bioconversion and transfer of mycotoxins from feed to milk[a].

Mycotoxin	Main product of rumen metabolism	Reduction of biological potency	Estimated carry-over rates
Aflatoxin B1	aflatoxicol	minor	n.d.[b] 0–12.4 $\mu g\,l^{-1}$[c]
	aflatoxin M_1[d]	minor	2.0–6.2%
Cyclopiazonic acid	unchanged	unchanged	n.d. 6.4–0.7 $\mu g\,l^{-1}$[e]
Fumonisin B1	unchanged	unchanged	0–0.05%
Ochratoxin A	ochratoxin-α	significant[f]	n.d.
T-2 toxin	various	significant	0.05–2%
DON (and related trichothecenes)	de-epoxy-DON (DOM)	significant	DON: 0.0001–0.0002 DOM: 0.0004–0.0024[g]
Zearalenone	α-zearalenol	none	0.06–0.08%[h]
Patulin[i]	unchanged	unchanged	n.d.
Ergovalin	unchanged	unchanged	n.d.
Lolitrem	unchanged	unchanged	n.d.

Note: [a]According to Galtier (1998, 1999), Yiannikouris and Jouany (2002), and other sources as indicated.
[b]n.d., Not determined.
[c]Aflatoxicol has been detected, however, in commercial milk samples (Carvajal et al. 2003).
[d]Aflatoxin M1 is not a product of rumen metabolism but originates from hepatic metabolism of aflatoxin B_1.
[e]According to Oliviera et al. (2006).
[f]Ochratoxin-α is considered to be less toxic than ochratoxin A, but it can be esterified to yield ochratoxin C, which is a toxic form.
[g]According to Seeling, Boghun et al. (2006).
[h]Total milk analysis shows also minor concentrations of β-zearalenol.
[i]Patulin is metabolised in the liver.

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references, see Jouany and Diaz 2005). These studies, addressing the transfer of mycotoxins into milk, have been conducted in healthy animals with an intact blood–milk barrier. However, various systemic diseases and local (mammary) infections might alter the functionality of this barrier and, hence, transmission rates may be higher in daily practice.

The blood–milk barrier comprises different anatomical structures and active transport processes. The physical barrier is formed by the epithelium of the blood capillaries that span and supply the secretory epithelium of the mammary gland. Polar substances and large molecules cannot pass this barrier by passive diffusion. Factors that determine the excretion with milk are the molecular weight and lipophilicity of a compound (including mycotoxins and their metabolites), as well as the degree of binding to plasma proteins, as only the unbound fraction can be transported. The transport rate is also influenced by the pH gradient between blood plasma and milk. In a healthy animal, the pH of milk is lower than the plasma pH, whereas in a diseased animal (suffering, for example, from mastitis) the pH of milk is equal to or even exceeds the blood plasma pH. These differences modulate the rate of transfer into milk as demonstrated for various drugs. Recently, a distinct class of transmembrane transporters, which facilitate the active excretion of endogenous and exogenous compounds from the bloodstream into milk, gains increasing attention. In the mammary gland, BCRC (the gene product of ABC transporter ABCG2) has been described as a major excretory transporter (Borst and Oude Elferink 2002). Substrates for these transporters are likely to appear in high concentrations in milk. Recently, it was shown that, for example, ochratoxin A is a substrate for BCRP (Schrickx et al. 2006), which correlates with the high prevalence of ochratoxin A in human breast milk samples. In addition, it has been shown that aflatoxin B1 is a substrate for BCRP, making it likely that aflatoxin M_1 and aflatoxicol are also excreted actively into milk (Van Herwaarden et al. 2006). These findings offer the possibility of estimating the likelihood of galactogenic excretion through rapid *in vitro* assays, which can be applied to all chemical classes of mycotoxins.

It is worthwhile mentioning that investigations devoted to the galactogenic excretion of various veterinary medicinal products did show significant differences in rumen metabolism and transfer into milk between individual ruminating species, such as dairy sheep, goats, and buffaloes (Merino et al. 2006). The increasing market for milk products from these animal species underlines the need for data from these animals as well.

The excretion of mycotoxins with milk is generally reviewed with respect to potential adverse effects on human health, particularly children, who are high milk consumers. Contamination of dairy milk with mycotoxins might, however, also impair milk quality and the use of milk for typical fermented dairy products such as yoghurt. As mentioned above, various mycotoxins, particularly those from silage moulds, exert strong antimicrobial effects. Even minor amounts of these toxins might affect milk technologies and the control of tank milk for undesirable residues of therapeutic antibiotics (false-positive results).

Current uncertainties in the assessment mycotoxins in the diet of dairy cows

The uncertainties in the exposure of dairy cows are attributable to significant differences in the composition of individual diets, depending on the feeding regimen, the availability of natural pastures, and the methods of feed preservation. Subsequently, the animals are potentially exposed to highly variable and complex mixtures of mycotoxins, and the health consequences of these mixtures are difficult to assess. Major points of interests are as follows:

- Various mycotoxins have the ability to modify the rumen flora due to their antimicrobial activity. This may decrease the degrading capacity of the rumen resulting in an unexpected passage rate of intact toxins from other sources. A comparable effect can be also be expected in cases in which the rumen flora is affected in the course of metabolic diseases, as, for example, rumen acidosis.
- Toxin–toxin interactions at the level of absorption and biotransformation are likely, but the clinical significance of these interactions remains to be elucidated.
- The excretion of mycotoxins with milk is generally low. Changes in the blood–milk barrier due to systemic, and particularly local, infections (mastitis) affect the integrity of the blood–milk barrier and the pH gradient between blood and milk. This may, in turn, alter the rate of excretion and facilitate the excretion of mycotoxins that are not expected in milk. As mentioned above, a number of recent reports refer to the likelihood that the excretion of mycotoxins influences the standard tests for undesirable residues of antibiotics in milk.
- Various mycotoxins exert a modulating effect on the immune system, even at low doses. This effect might result in an increased prevalence of infectious diseases

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or an acceleration of minor infections. An increased incidence of mastitis and lower leg problems in dairy cows has been associated with a poor quality of the given silage (Nyman et al. 2007). To what extend this phenomenon is directly attributable to mycotoxins in the silage needs to be investigated.

In conclusion, dairy cows are protected against exposure to mycotoxins by their rumen flora. Various mycotoxins, however, pass this barrier or are converted into metabolites that retain biological activity. The assessment of undesirable effects exerted in ruminants should include the antimicrobial activity of various mycotoxins that results in an impairment of the function of the rumen flora, followed by a poor feed utilization and reduced weight gain and productivity.

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