IMPACT OF MYCOTOXINS ON THE HEALTH AND PRODUCTIVITY OF DAIRY CATTLE

G.B. Penner
Department of Animal and Poultry Science
University of Saskatchewan

INTRODUCTION

The term mycotoxin covers a broad group of secondary metabolites produced by fungi. By definition, these metabolites must be toxic in nature to the species of focus; in this case dairy cattle. That said, not all fungal metabolites are considered to be mycotoxins. Mycotoxins of interest include aflatoxins, ergot alkaloids, fumonisins, ochratoxins, patulin, trichothecenes, and zeralenone (Bennet and Klich, 2003). Past research has focused on cereal grains, byproducts, and dry-stored forage as primary sources of mycotoxins, however, ensiled feeds can also be prominent source for dairy cattle (Driehuis et al., 2008). This review will focus on mycotoxin degradation in the rumen and the effects of mycotoxins on gastrointestinal function. Production responses will also be highlighted.

Ruminal degradation of mycotoxins and the effect of mycotoxins on gastrointestinal function

There is no doubt that ruminants have greater tolerance to feed contaminated with mycotoxins than monogastrics. The improved resistance is largely related to the ability of the ruminal microflora to degrade mycotoxins converting them into less potent intermediates (Hussein and Brasel, 2001; Fink-Gremmels, 2008). For example, ochratoxin is degraded into ochratoxin α and phenylalanine by mixed microbes isolated from the reticulo-rumen and omasum; both of which have reduced toxicity (Hult et al., 1976). Kiessling et al. (1984) evaluated the degradation of aflatoxin, ochratoxin, zearalenone, T-2 toxin, diacetoxyscirpenol (**DAS**), and deoxynivalenol (**DON**) using in vitro incubation with mixed rumen microbes or with protozoa, or bacteria alone. That study led to several important findings. Firstly, ochratoxin degrading activity appears to respond to feeding cycles with lowest activity immediately after a meal and greatest activity prior to the meal. Secondly, the greatest ochratoxin, zearalenone, DAS, and T-2 toxin was found for the protozoa rich incubation (Hussein et al., 2001; Fink-Gremmels, 2008). In contrast, Keissling et al. (1984) found that aflatoxin and DON were not degraded in vitro. The lack of ruminal degradation of aflatoxin has been confirmed by subsequent studies (Westlake et al., 1989; Hussein et al., 2001) while degradation of DON appears to be variable (Westlake et al., 1989) with nearly complete degradation being predicted in vivo using cattle fitted with a duodenal cannula (Dänicke et al., 2005). Finally, the Keissling et al. (1984) study reported that when sheep were fed a high-grain diet, capability for toxin degradation was reduced by 20%. This may suggest that dietary scenarios that partially defaunate the rumen may decrease the ability of microbial

degradation of mycotoxins and thereby reduce tolerance of ruminants to mycotoxins in feed.

Microbial degradation may not be sufficient to reduce the potency of all mycotoxins. Despite some degradation of ergot alkaloids by ruminal microbes to yield lysergic acid (Duringer et al., 2007), lysergic acid may be transported across the gastrointestinal tract at a greater rate than most ergot alkaloids suggesting that the overall toxic dose may not be reduced (Guerre, 2015). Moreover, while there is degradation of ergot alkaloids, there was 35% recovery of ergovaline in feces from sheep and nearly 250% recovery of lysergic acid (DeLorme et al. 2007). This suggests that despite some capacity for degradation, exposure of gastrointestinal tissues and potentially systemic tissues to ergot alkaloids is possible. T-2 toxin is catabolized to HT-2 toxin and zeralenone is degraded to zeralenol (among others). Zeralenol has a greater affinity to estrogen receptors than zeralenone demonstrating that microbial degradation can, at times, worsen the challenge (Marczuk et al., 2012). In addition, the role of microbes to degrade mycotoxins may come at a cost as there is clear evidence demonstrating that mycotoxins may alter the ruminal microflora activity. High doses of aflatoxin B_1 and G_1 (1.0 µg/mL of rumen fluid) reduced DM digestion of hay by 50 and 20% respectively (Westlake et al., 1989). El-Ayouty and El-Saadany (1990) as well as others (Escoula, 1992; Puel et al., 2005) also reported reductions in DM and OM digestibility associated mycotoxin contaminated feed. Perhaps this is not surprising given that some mycotoxins are known to have antimicrobial properties (Fink-Gremmels, 2008; Strickland et al., 2011). Future studies should evaluate the impact of mycotoxins on the ruminal microbiome to evaluate species that increase and decrease in relative abundance when exposed to mycotoxins.

Corresponding to antimicrobial properties of some mycotoxins, May et al. (2000) evaluated the effect of DON and fusaric acid on *Ruminococcus albus* and *Methanobrevibacter ruminantium*. Fusaric acid inhibited the growth of *R. albus* and *M. ruminantium* with concentrations as low as 15 µg/mL while DON had no effect. Fumonsin B_1 was reported to have little influence on short-chain fatty acid production and microbial activity; however, it should be noted that only 12 to 18% of the fumonsin B_1 was degraded after 72 h of incubation (Caloni et al., 2000). Feeding mycotoxin contaminated grain has also been reported to increase ruminal ammonia concentration and reduce the microbial protein flow the small intestine (Dänicke et al., 2005).

Mycotoxins such as slaframine (Froetschel et al., 1986) and ergot alkaloids (Koontz, 2015) can directly impact rumen function. Froetschel et al. (1986) reported marked reductions in rumen motility and increases in rumen fluid volume and rumen liquid outflow (Froetschel et al., 1987). Ergot alkaloids can bind with G-protein coupled receptors, beta-adrenergic receptors, and biogenic amine receptors (Koontz, 2015). The ability of ergot alkaloids to act as ligands for a variety of receptors presents a challenge for a clear diagnosis in field conditions. However, reduced serum prolactin is a common response. Cattle fed feed contaminated with ergot alkaloids also have reduced blood flow caused by vasoconstriction and consequently reduced SCFA absorption from the rumen (Foote et al., 2012). The reduction in SCFA absorption appears to be largely in

response to the reduced blood flow and low feed intake (Foote et al., 2012) and independent of epithelial function as exposure to ergovaline ex vivo did not alter SCFA transport despite the ability to detect the movement of ergovaline across the isolated ruminal epithelia in under the same model (Foote et al., 2014). Interestingly, exposure of the rumen epithelium to 50 or 250 ng ergovaline/mL did not alter barrier function of the ruminal epithelium. It is not clear whether other mycotoxins, such as patulin (Mahfoud et al., 2002) or fumonsin B1, alter barrier function of the gastrointestinal tract in ruminants as reported for monogastrics.

In monogastrics, it is known that species differ for the potential to absorb mycotoxins across the gut with rapid rates for aflatoxins, poor intestinal absorption for fumonsins, and moderate for DON (Grenier and Applegate, 2013). However, entero-hepatic recycling via the bile may contribute to increased exposure of intestinal epithelial cells to mycotoxins and mycotoxin incorporation into micelles may increase intestinal absorption (D'Mello et al., 1999; Mahfoud et al., 2002; Grenier and Applegate, 2013). Indeed, DON has been shown to reduce the absorptive surface area in poultry (Awad et al., 2006a, Awad et al., 2006b, Awad et al., 2011). Supporting the reduction in absorptive surface area, Awad et al. (2007) also noted that DON inhibited the glucose-dependent increase in short-circuit current of the jejunum in Ussing chambers. This suggests that DON, and potentially other mycotoxins, may modulate sodium transport by intestinal epithelium. Given the potential for detoxifying effects in the rumen, it would be expected that the effective dose ingested to induce such effects in ruminants would be much greater than monogastrics, but it could be expected that similar responses would occur. Others have also shown a reduction in Na-dependent transport processes with ochratoxin (Maresca et al. 2001), and DON (Maresca et al., 2002). Thus, it appears that mycotoxins have the potential to alter Na-dependent nutrient absorption in monogastric species but to the authors' knowledge, there is no work evaluating similar processes in ruminants. As stated above, addition of ergovaline was not reported to alter SCFA transport ex vivo (Foote et al., 2014) suggesting that reduced blood flow was the primary mechanism decreasing SCFA absorption in vivo (Foote et al., 2013).

In addition to reduced nutrient transport capability, there is evidence in monogastric species demonstrating that exposure to ochratoxin, fumonsin B1, and DON can reduce trans-epithelial resistance thereby increasing the paracellular permeability of the intestinal epithelium (Grenier and Applegate, 2013). It appears that basolateral exposure to DON down-regulates tight-cell junction associate proteins (zona occludin-1 and occludin) suggesting that movement of DON across the epithelia may be required to induce negative effects on barrier function. As with nutrient absorption, data is limited on whether such a response occurs in ruminants.

Effect mycotoxins on the productivity of dairy cattle

The symptoms of mycotoxin exposure for dairy cattle are general and vague. Symptoms include low feed intake, reduced milk production, exacerbated negative energy balance, and hemorrhagic enteritis and diarrhea, reproductive failure, mastitis, and laminitis (Fink-Gremmels, 2008; Marczuk et al., 2012). Given the non-specific

symptoms, variation in mycotoxin concentration in feeds, and diagnostic challenges, confirming chronic mycotoxin exposure is difficult. (Fink-Gremmels, 2008) suggested that exposure to aflatoxins may reduce liver function and contribute to development of fatty liver disease, especially for cows in early lactation. However, a recent case-study report in Poland (Marczuk et al., 2012) demonstrated detectable plasma concentrations of DON and elevated levels of zeralenone. The exposure to DON and zeralenone was prolonged and 5 cows died during the study. Associated with the elevated plasma DON and zeralenone, was an increase in PCV, Ca, and leukocytosis.

Although mycotoxins are often implicated with reduced milk production, supporting evidence is difficult to find in published literature. Studies evaluating adsorbants as a strategy to reduce the impact of mycotoxins have reported that low doses of mycotoxins likely do not affect DMI or milk production (Xiong et al., 2015). For example, Queiroz et al. (2012) reported that a diet containing 75 µg/kg aflatoxin B1, did not affect DMI or milk yield for dairy cattle but decreased the concentration of milk CP supporting the inhibitory effect of aflatoxin on protein synthesis. Firmin et al. (2011) reported no effect of aflatoxin B1 or M1 on DMI, milk yield but reduced milk fat content for sheep. Even long-term exposure to DON did not affect hepatic function in dairy cattle (Kinoshita et al., 2015). While aflatoxin and trichothecenes seem to have little effect on DMI and milk yield but reduce milk CP, ergot alkaloids have a potent effect to reduce milk yield. Early work in rats demonstrated that administration of a variety of ergot alkaloids inhibited prolactin secretion thereby inhibiting lactation (Shaar and Clemens, 1971). Work in pre-partum heifers (Bernard et al., 1993) and cows supported these findings demonstrating that even pre-partum exposure to endophyte infected fescue decreased prolactin concentration prior to parturition; however, prolactin concentrations recovered and milk yield was only numerically lower for cows exposed to alkaloids relative to their counterparts. Part of the discrepancy between anecdotal field evidence and controlled research studies may be related to the additive effect of multiple mycotoxins present in feeds at once compared to the single or dual mycotoxin evaluation treatments that have been investigated in research studies and perhaps the duration of the exposure.

CONCLUSIONS

Ruminants have a greater tolerance to mycotoxins than monogastrics due to ruminal metabolism. However, potential effects of mycotoxins on intestinal epithelial cells may still be present although there is limited data to support the outcomes in dairy cattle. Although mycotoxins have been suggested to affect DMI and milk yield, there is limited data to support such a conclusion. Future work is needed to evaluate combinations of mycotoxins on production parameters.

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