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Invited Review

Kinetics and metabolism of the *Fusarium* toxin deoxynivalenol in farm animals: Consequences for diagnosis of exposure and intoxication and carry over

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ABSTRACT

The knowledge of factors influencing the kinetics, metabolism and bioavailability of the *Fusarium* toxin deoxynivalenol (DON) is a basic prerequisite for evaluation of the transfer (carry over) of the toxin and its metabolites into edible tissues, and for a physiological specimen-based diagnosis of intoxication. These aspects are addressed in the present review, and potentials and pitfalls of the suitability of analysis of physiological samples for evaluation of the DON exposure as a veterinary tool are discussed. For example, the farm animal species was shown to be a determining factor influencing the metabolic profile and the bioavailability of DON. Although linear relationships were derived between DON exposure of *ad libitum* and restrictively fed animals and DON or de-epoxy-DON concentration in the blood of pigs, dairy cows and sheep, it has to be considered that individual values might markedly deviate from these relationships, which makes interpretation of measured concentrations of DON and its metabolites difficult. The situation is further complicated by the lack of established relationships between DON residues in physiological matrices and the adverse effects of DON on the health and performance of farm animals.

Contents

1. Introduction

The importance of the mycotoxin deoxynivalenol (DON) as a common contaminant of feed for farm animals has been recog-

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nized by the European Feed Safety Authority (EFSA, 2004). Based on this EFSA opinion the Commission of the European Communities (CEC) established so-called guidance values for critical concentrations of DON and further mycotoxins in feed materials and complete feeds (CEC, 2006). These guidance values are intended to protect farm animals from possible deleterious effects of contaminated feed, and to ensure the awareness of all economic parties and supervisory authorities if these critical concentrations are exceeded, in order to identify the sources and to close them. The DON guidance values for complete feed reflect the species-specific sensitivity. The lowest guidance value of 0.9 mg/kg complete feed was established for all categories of pigs as the most sensitive farm animal species. Calves (<4 months of age), lambs and kids are considered to be protected if complete feed DON concentrations do not exceed 2 mg/kg, while 5 mg/kg applies for other farm animal species and categories, including ruminants, horses and poultry.

Toxic effects of DON on farm animals were repeatedly reviewed (Döll and Dänicke, 2011; EFSA, 2004; Rotter et al., 1996) with the anorectic and immune-modulatory effects being most pronounced in pigs. For example, through a literature compilation, a mean decrease in voluntary feed intake of 5% was estimated per 1 mg increase in the dietary DON concentration. The immune-modulatory effects of DON, as repeatedly demonstrated in mice exposed to high DON doses, could not consistently be reproduced in pigs fed diets with DON concentrations relevant for practical feeding conditions (Döll and Dänicke, 2011).

Besides the evaluation of the actual DON exposure through feed analysis, the detection of DON in physiological samples such as blood and bile are frequently discussed as diagnostic tools. However, the applicability of this tool requires not only the analytical detection of the native toxin DON but also that of possible DON degradation products, which arise after ingestion of DON-contaminated feed. The situation is further complicated by the fact that the profile and the kinetics of these degradation products, which are often collectively referred to as to DON metabolites, vary with species, age and nutritional situation.

The aim of this review is to discuss the metabolism and kinetics of DON for the most important farm animal species with a special focus on pigs and on diagnostic opportunities.

2. Metabolism

Generally, the term "metabolism" of DON or of other mycotoxins is used to describe the conversion of the native toxin to various degradation derivatives occurring in both the digestive tract, as mediated by microbes, and in the organism, where intestinal mucosa, liver, and kidneys are the major players in phase II metabolism. Derivatives of DON include its microbially metabolised de-epoxidized form, called de-epoxy-DON, DOM-1 (DON metabolite 1; Yoshizawa et al., 1983) or simply de-DON, and their conjugated forms as a result of the phase II metabolism (Fig. 1).

2.1. De-epoxidation

The incubation of rumen fluid with increasing DON concentrations resulted in a time-dependent decrease of DON and an evolution of de-epoxy-DON. The latter was found to be the only degradation product of DON (King et al., 1984, Fig. 2). Similarly, de-epoxidized DON and nivalenol were detected after the anaerobic incubation of rumen fluid (He et al., 1992; Hedman and Pettersson, 1997; Swanson et al., 1987), underscoring the role of intestinal microbes in transforming DON to de-epoxy-DON. The role of the rumen in de-epoxidation of DON has been addressed in several *in vivo* experiments with sheep and cows. Interestingly, the ruminal conversion rate from DON to de-epoxy-DON was estimated to reach approximately 15% in sheep dosed singly with DON, which is considerably lower than reported for dairy cows. Two studies measuring the flow of DON and de-epoxy-DON at the proximal duodenum in dairy cows fed DON-containing diets for several weeks revealed that a much higher percentage of ingested DON left the rumen as de-epoxy-DON. Under such conditions of a longer DON exposure time of several weeks, the major portion of 81–93% (Dänicke et al., 2005b) and 94–99% (Seeling et al., 2006) of the total flow of DON plus de-epoxy-DON were in the form of the de-epoxidized metabolite. Despite this high de-epoxidation degree, the total flow of DON plus de-epoxy-DON accounted only for 4–28% and 12–77% of DON-intake, respectively. This incomplete recovery of ingested DON at the duodenum suggests either absorption of DON and/or de-epoxy-DON across the rumen epithelia or a complete degradation by rumen microbes. Compared to the rumi-

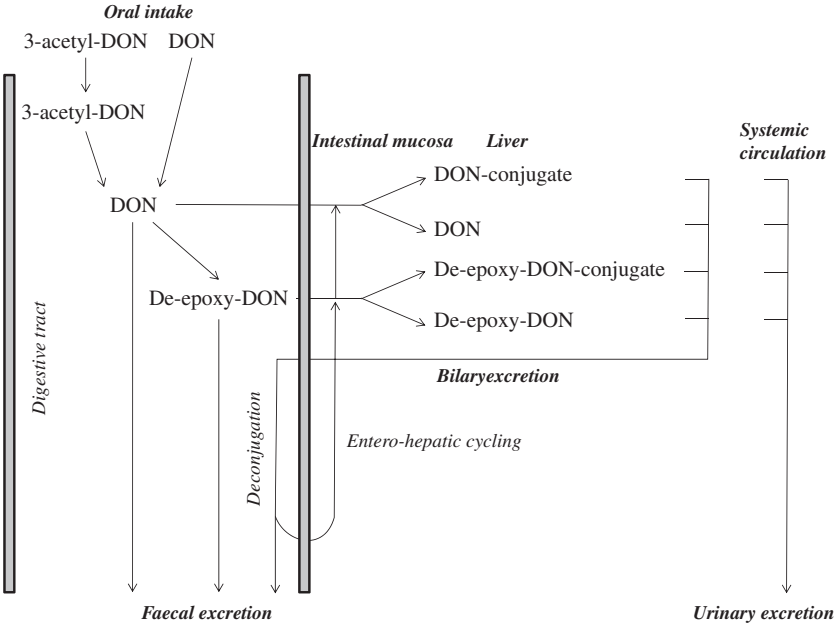

Fig. 1. Metabolism of DON in pig and cattle.