# Bioavailability of the *Fusarium* toxin deoxynivalenol from naturally contaminated wheat for the pig*

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## INTRODUCTION

The *Fusarium* toxin deoxynivalenol (DON) is of outstanding importance for human and animal health because of its frequent occurrence in toxicologically relevant concentrations. However, only limited data of the toxicokinetic parameters of pure DON in pigs are available. Therefore, the present study aimed to determine the bioavailability of DON from a naturally contaminated source and to distinguish the effects of an acute and chronic DON intoxication.

## MATERIALS AND METHODS

16 castrated male pigs (41.5 ± 2.0 kg) were provided with a permanent catheter to facilitate frequent blood sampling (0, 5, 10, 15, 20, 30, 45, 60, 90, 120 min, then every hour until 12 h, and after 24h). The toxicokinetics of DON from naturally *Fusarium* contaminated wheat (16.6 mg DON/kg, in a diet with a total wheat content of 40 %) was examined after chronic exposure (≥ 4 weeks) or a single oral dose (acute).

The systemic absorption (bioavailability) of DON was estimated based on the area under the curves (AUC) after dietary exposure and intravenous application of pure DON (53 µg/kg bw).

***Table 1.*** *Design and number of pigs of the studies*

| Study | Group | DON application | | N | Mean dose |
|---|---|---|---|---|---|
| | | Duration | Form | | (µg/kg bw/d) |
| **Kinetic** | DON chronic | 5-8 weeks | Wheat | 5 | 68.5 ± *4.9* |
| | DON acute | Single bolus | Wheat | 6 | 77.3 ± *2.4* |
| | DON iv | Single bolus | crystalline | 5 | 53.0 ± *0.0* |
| **Balance** | Control | - | - | 11 | 4.2 ± *0.4* |
| | DON chronic | 4-6 weeks | Wheat | 11 | 162.9 ± *15.9* |

DON and its metabolite de-epoxy-DON was determined in serum, urine and freeze-dried faeces according to Valenta et al. (2003).

## RESULTS

Following intravenous dosing, the disappearance of DON is described by a two compartment model, while the oral dosing was characterized by an first-order absorption and elimination (Figure 1).

***Table 2.*** *Toxicokinetic parameters after chronic and acute oral or intravenous (iv) DON exposure*

| | DON iv | DON chronic | DON acute |
|---|---|---|---|
| **Live weight [kg]** | **39.7** ± *0.8* | **42.4** ± *2.3* | **41.6** ± *2.3* |
| **$C_{max}$ [ng/ml]** | | **21.8** ± *3.4* | **15.2** ± *3.3* |
| **$t_{max}$ [h]** | | **1.5** ± *0.5* | **1.7** ± *0.8* |
| **t½α [h]** | **0.7** ± *0.5* | **0.4** ± *0.3* | **0.7** ± *0.6* |
| **t½β [h]** | **15.2** ± *12.9* | **6.3** ± *2.4* | **5.3** ± *2.4* |
| **$V_d$ [l/kg]** | **3.8** ± *2.3* | **2.7** ± *0.6* | **4.0** ± *1.7* |
| **Cl [ml/kg*min]** | **3.8** ± *1.6* | **5.3** ± *1.6* | **9.3** ± *2.9* |
| **$DON_{conjugated}$ [%]** | **-4.8** ± *15.2* | **14.2** ± *33.5* | **35.6** ± *20.8* |
| **$F_{free\ DON}$ [%]** | **100.0** ± *13.5* | **89.4** ± *27.2* | **54.1** ± *17.6* |
| **$F_{total\ DON}$ [%]** | **100.0** ± *12.0* | **112.3** ± *24.2* | **91.5** ± *27.4* |

$C_{max}$, maximum serum DON concentration; $t_{max}$, time of maximum serum DON concentration; t½α, biological half-life of distribution (iv) or absorption (oral); t½β, half-life of elimination; $V_d$, apparent volume of distribution; Cl, clearance; F, bioavailability of free and total (free + conjugated) DON.

DON was found in serum of pigs as early as 15 min after feeding a DON contaminated meal, with peak concentrations between 0.8 to 2.3 h (Table 2). DON was highly distributed in all groups, with an apparent volume of distribution ($V_d$) higher than the total body water. After dietary DON exposure 9 to 60 % of total (free + conjugated) DON was in the form of the glucuronid conjugate, while following iv application DON in serum seemed not to be conjugated. The mean bioavailability (F) of free (unconjugated) and total (free+conjugated) DON was 89 and 112 % for the chronic group and 54 and 92 % for the acute oral group, respectively.

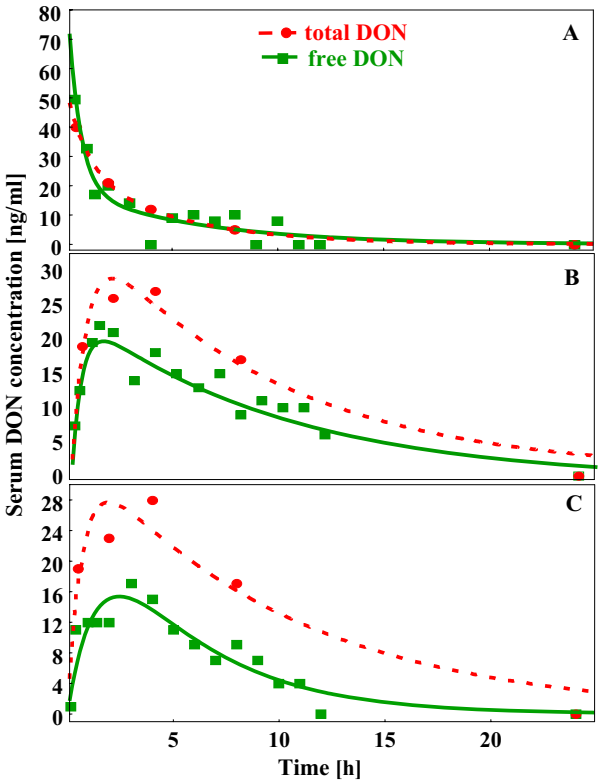


***Figure 1.*** *DON concentrations in serum [ng/ml] of one exemplary pig dosed intravenously with 53 µg DON/kg bw (A) or fed a DON contaminated diet (5.7 mg/kg) chronically (B) or acutely (C).*

## CONCLUSIONS

In the present study, oral exposure of a diet contaminated naturally with DON resulted in a rapid and nearly complete (total DON) absorption, high distribution and low metabolism. The difference in the glucuronidation grade between oral and iv DON exposure might indicate a glucuronidation within the intestinal tract. However, the effects of glucuronide conjugation of DON on toxicity and excretion behavior in pigs have to be clarified. Assuming a high comparability of digestion and excretion in humans and swine, it can be concluded that although DON is poorly detoxified, it is rapidly excreted and is not found in remarkable concentrations in serum after 24 h.

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