# Metabolization and renal excretion of deoxynivalenol and its glucoside.

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Due to the lack of information about DON absorption and excretion, the aims of this study are the description of the DON and metabolites excretions patterns and know the absorption and excretion rates of it. Moreover, the results can be useful to...

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|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving nog niet gestart |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON24752

**Bron**
Nationaal Trial Register

**Verkorte titel**
Deoxynivalenol = DON

**Aandoening**

Deoxynivalenol
Excretion

### Ondersteuning

**Primaire sponsor:** Foodball project and Research Foundation Flanders (FWO)
**Overige ondersteuning:** Foodball project and Research Foundation Flanders (FWO)

### Onderzoeksproduct en/of interventie

### Uitkomstmaten

**Primaire uitkomstmaten**

Urine collection for 24 h

# Toelichting onderzoek

### Achtergrond van het onderzoek

Deoxynivalenol (DON), also known as vomitoxin, is a mycotoxin that acts as a potent inhibitor of protein synthesis, stimulates the pro-inflammatory response, cause ribotoxic stress, cytotoxicity and apoptosis, resulting on the impairment of multiple physiological functions, such as the intestinal barrier, growth, immune regulation or reproduction. Furthermore, this mycotoxin has been linked with animal and human gastroenteritis outbreaks due to acute exposition (Pestka, 2010). Despite its toxicity, DON is a highly common mycotoxin in cereals and cereals products ((De Boevre, et al., 2012; Marin, Ramos, Cano-Sancho, & Sanchis, 2013) Marin et al., 2013) and as a result it is one of the major mycotoxins in our diets. Thus, exposition studies showed the large exposure of human to this toxin with high percentages of population exceeding the tolerable daily intake (TDI) (Heyndrickx, et al., 2015; Vidal, Cano-Sancho, Marin, Ramos, & Sanchis, 2016).

Furthermore, free mycotoxins, like DON, might not be the only hazard for consumer's health, because the so-called modified mycotoxins are also widely common in food. Modified mycotoxins are toxins attached to more polar functional groups, such as glycosyl residues or sulfates, or to polymeric carbohydrates or protein matrices (Berthiller, Schuhmacher, Adam, & Krska, 2009; Rychlik, et al., 2014). The modified mycotoxins may have plant, fungal, mammalian and food processing origins. A major concern and potential risk for consumers is the possible hydrolysis of modified mycotoxins into their toxic free forms during mammalian digestion (Broekaert, et al., 2015; Grabley, Gareis, Bockers, & Thiem, 1992; V. Nagl, et al., 2014). Contrary to the wealth of information on the free mycotoxins, only limited data are available for mycotoxin derivatives in foods. The co-occurrence of free and modified DON forms has been documented in raw wheat, especially with focus on deoxynivalenol-3-glucoside (DON-3-glucoside), 3-acetyldeoxynivalenol (3-ADON) and 15-acetyldeoxynivalenol (15-ADON). Reported levels of DON-3-glucoside are variable, however, the concentration of DON-3-glucoside can be high and even the same as DON in processed cereals (De Boevre, et al., 2012). 3-ADON and 15-ADON have also been detected in cereals and cereals products with a lower incidence than DON-3-glucoside (De Boevre, et al., 2012). (Berthiller, et al., 2011) demonstrated that several lactic acid bacteria hydrolyse DON-3-glucoside in vitro, which has been a first step to prove the toxicological relevance of DON-3-glucoside. On the other hand, 3-ADON and 15-ADON are rapidly converted to DON during digestion (Broekaert, et al., 2015; Versilovskis, et al., 2012). Thus, due to the high presence of DON conjugates in food and the easy transformation of them to DON, the FAO/WHO Expert Committee (JEFCA) considered DON-3-glucoside to be an additional contributing factor to total dietary exposure to DON (JECFA, 2010).

To know the DON exposition, analysis of urinary levels of DON has been proposed due to its short excretion half-life. However, different studies showed that DON glucuronides, which are the main phase II metabolites of DON, are the most common DON form in urine, specially DON-3-glucuronide and DON-15-glucuronide (Warth, et al., 2012). So, the analysis of glucuronides forms in urine is crucial for the study of trichothecenes biomarkers, because

about 90 % of DON excreted via urine is conjugated with glucuronic acid. For the glucuronides determination, a preliminary approach was developed based on the breakage of deoxynivalenol-glucuronides and subsequent determination of “total deoxynivalenol” (sum of free and released mycotoxins by hydrolysis). Afterwards, a direct method for quantification of glucuronides such as deoxynivalenol-3-glucuronide and deoxynivalenol-15-glucuronide was developed. The analytical developments permitted to find strong correlations between the sum of urinary deoxynivalenol and its glucuronidated metabolites (Turner, White, et al., 2010; Warth, Sulyok, Berthiller, Schuhmacher, & Krska, 2013). These investigations revealed the power of biomarker driven work when compared to traditional exposure assessment by analyzing food stuff. However, the analysis of DON in urine presents some uncertainties and limitation to fully validate the DON excretion metabolism and renal excretion. Firstly, biomonitoring data may depend on the moment in time when the sample is collected (Clewell, Tan, Campbell, & Andersen, 2008). Furthermore, there is a lack of information in the absorption and excretion rate of it. Finally, the high presence of DON conjugates in food like DON-3-glucoside or acetyl-deoxynivalenol (ADONs) add more uncertainties for the correlation between urinary DON and DON intake.

**Doel van het onderzoek**

Due to the lack of information about DON absorption and excretion, the aims of this study are the description of the DON and metabolites excretions patterns and know the absorption and excretion rates of it. Moreover, the results can be useful to build an standardized method to estimate deoxynivalenol-intake by means of biomarkers.

**Onderzoeksopzet**

3 days of diet without cereals at day 3 DON or DON-3-glucoside administration

**Onderzoeksproduct en/of interventie**

Diet without cereals

DON and DON-3-glucoside administration at TDI level.

# Contactpersonen

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

All adult people

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Pregnant or breestfeeding women

People with kidney or liver problems

Children and babies.

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Cross-over |
| Toewijzing: | Gerandomiseerd |

**Controle:** Placebo

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving nog niet gestart |
| (Verwachte) startdatum: | 01-02-2017 |

| | |
|---|---|
| Aantal proefpersonen: | 20 |
| Type: | Verwachte startdatum |

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 08-12-2017 |
| Soort: | Eerste indiening |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL6668 |
| NTR-old | NTR6902 |
| Ander register | JPI Food Biomarkers Alliance (FOODBALL) project. : G0D4615N |

## Resultaten