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RIJKSINSTITUUT VOOR VOLKSGEZONDHEID EN MILIEU
NATIONAL INSTITUTE OF PUBLIC HEALTH AND THE ENVIRONMENT

RIVM report 388802 018

Deoxynivalenol

Derivation of concentration limits in wheat and wheat containing food products

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With contributions of J.D. van Klaveren and M.M.H. van Dooren (RIKILT)

October 1999

This investigation has been performed by order and for the account of Ministry of Health, Welfare and Sport, within the framework of project 388802, ‘Natural toxins’.

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Abstract

The mycotoxin deoxynivalenol (DON) produced by fungi of the *Fusarium* genus may occur in various cereal crops. To calculate concentration limits for DON in wheat and wheat containing food products, a provisional TDI of 1.1 μg per kg body weight is derived. Children (1-4 yr.) have the highest wheat consumption per kg body weight per day and form the population at risk. To derive a safe concentration limit of (cleaned) wheat, we assumed a child with a high wheat consumption. Based on the wheat content of food products and the derived concentration limit for DON in (cleaned) wheat, concentration limits for various food products are calculated.
The following general concentration limits are proposed: 120 μg DON/kg for (cleaned) wheat, 60 μg DON/kg for bread and 120 μg DON/kg for food products with a wheat content > 33%. It is suggested to monitor only the (cleaned) wheat for food products with a wheat content < 33%.

Contents

Samenvatting

Onlangs zijn in Nederland hoge concentraties van het mycotoxine deoxynivalenol (DON) aangetroffen in tarwe en tarwebevattende voedingsmiddelen. Het RIVM/CSR is gevraagd om een risicobeoordeling van DON uit te voeren en om concentratielimieten voor tarwe en tarwebevattende voedingsmiddelen te berekenen. Gebaseerd op literatuurgegevens is een voorlopige toelaatbare dagelijkse inname (TDI) van 1.1 μg per kg lichaamsgewicht afgeleid. Het meest kritische effect is groeivertraging. Zowel op basis van dit effect als op basis van tarweconsumptiegegevens, geleverd door het RIKILT, wordt in geval van DON de risicogroep gevormd door kinderen (1-4 jaar). Deze consumeren 4.5 – 8.5 g tarwe per kg lichaamsgewicht per dag. De consumptie van brood is verantwoordelijk voor circa 70% van de totale tarwe-inname. Ontbijtgranen, koekjes en pasta dragen voor circa 17% aan de totale tarwe-inname van kinderen bij. Om veilige concentratielimieten af te leiden, is uitgegaan van een hoge tarweconsumptie (i.e., 8.5 g/kg lichaamsgewicht, overeenkomend met het 95^{e} percentiel). Gebaseerd op het tarwegehalte van voedingsmiddelen en de afgeleide concentratielimiet voor DON in (geschoonde) tarwe, zijn de concentratielimieten voor verscheidene voedingsmiddelen berekend. Hierbij is geen rekening gehouden met mogelijke DON-contaminatie van granen anders dan tarwe (b.v. haver, rogge, gerst).

Teneinde handhavingsactiviteiten te vergemakkelijken, worden de volgende algemene concentratielimieten voorgesteld: 120 μg DON/kg voor (geschoonde) tarwe, 60 μg DON/kg voor brood en 120 μg DON/kg voor voedingsmiddelen met een tarwegehalte > 33%. Aanbevolen wordt om voedingsmiddelen met een tarwegehalte < 33% te monitoren op basis van de (geschoonde) tarwe.
Uitgaande van de algemene concentratielimieten en het consumptiepatroon van kinderen die tarwebevattende voedingsmiddelen werkelijk gebruiken, bedraagt de dagelijkse DON inname 76% en 106% van de voorlopige TDI voor jongens respectievelijk meisjes. NB: de beschouwde voedingsmiddelen dragen voor circa 80% aan de totale tarwe inname bij.
In geval dat de voorgestelde algemene concentratielimieten niet haalbaar zijn, kunnen hogere concentratielimieten noodzakelijk of onvermijdbaar worden geacht. Om de bovengenoemde veilige concentratielimieten af te leiden, is uitgegaan van een kind met een hoge (95^{e} percentiel) tarweconsumptie. Een lager percentiel zou tijdelijk acceptabel kunnen worden geacht, aangezien het meest relevante toxische effect (groeivertraging) beschouwd kan worden als een reversibel effect. Gebaseerd op een mediane tarwe-inname (50^{e} percentiel) van 4.5 g tarwe per kg lichaamsgewicht per dag, worden tweevoudig hogere concentratielimieten verkregen.

Summary

Recently, high contamination levels of the mycotoxin deoxynivalenol (DON) have been detected in wheat and in wheat containing food products in the Netherlands. Therefore, RIVM/CSR was requested to carry out a risk evaluation on DON and to calculate concentration limits in wheat and wheat containing food products.
Based on the literature on DON-toxicity, a provisional TDI of 1.1 μg per kg body weight is derived. The most critical effect was growth retardation. Based on this critical effect as well as on wheat consumption data, provided by RIKILT, the population at risk consists of children (1-4 yr.). Children consume 4.5 – 8.5 g wheat per kg body weight per day. The consumption of bread contributes for approximately 70% to the total wheat intake. Breakfast cereals, cookies and pasta contribute for approximately 17% to the total wheat intake of children. To derive safe concentration limits, we assumed a high wheat intake (i.e. 8.5 g/kg body weight, which is the 95th percentile). Concentration limits for various food products are calculated based on the wheat content of food products and the derived concentration limit for DON in (cleaned) wheat. Possible DON-contamination of grains other than wheat (e.g. oat, rye, barley) has not been taken into account.

To facilitate governmental surveillance and enforcement activities the following general concentration limits are proposed: 120 μg DON/kg for (cleaned) wheat, 60 μg DON/kg for bread and 120 μg DON/kg for food products with a wheat content > 33%. For food products with a wheat content < 33% it is suggested to monitor only the (cleaned) wheat used as an ingredient.
Considering the general concentration limits and the consumption profile of children who actually use these wheat containing food products, the daily DON intake equals 76% and 106% of the provisional TDI (girls and boys, respectively). Please note that the considered food products contribute to approximately 80% of the total wheat intake.
If the proposed general concentration limits are difficult to enforce, higher concentration limits may be considered necessary or unavoidable. To derive the safe concentration limits mentioned above we assumed a child with a high (95th percentile) wheat consumption. A lower percentile may be considered temporarily acceptable since the most relevant toxic effect (growth retardation) is a reversible effect. Based on a median wheat intake (50th percentile) of 4.5 g wheat per kg body weight per day, two-fold higher concentration limits are derived.

1. Introduction

The mycotoxin deoxynivalenol (DON) produced by fungi of the *Fusarium* genus may occur in various cereal crops. Recently, high contamination levels of DON have been detected in wheat and in wheat containing food products in the Netherlands. The Ministry of Public Health, Welfare and Sports (VWS) requested RIVM/CSR to carry out a risk evaluation on DON. For this purpose toxicity studies carried out with DON have been critically evaluated. In Appendix 1 'Toxicology' a provisional TDI for DON is derived. Based on a NOAEL of 0.11 mg DON per kg body weight per day in a chronic mouse study, the provisional TDI for humans is set on 1.1 μg per kg body weight.

Since contaminated wheat is consumed through a large variety of wheat containing food products, the Ministry of VWS subsequently requested RIVM/CSR to derive concentration limits for wheat containing food products. For this, we considered the consumption of wheat in the Netherlands, the population at risk and the contribution of various food products to the total wheat intake. We assumed that wheat forms the major source of DON-uptake in the Netherlands. Therefore, possible DON-contamination of cereal grains other than wheat (e.g. oat, rye, barley) has not been taken into account.

In the case of exposure to DON the population at risk consists of children in the age of 1-4 year. The reason for this is twofold. Firstly, children (1-4 year) have the highest wheat intake when expressed as g per kg body weight per day, i.e. 4.5 – 8.5 g/kg body weight per day *(VCP-3 1997-1998).* Secondly, one of the toxic effects of DON in experimental animals is growth reduction. Especially fast growing children will be vulnerable to this type of toxic effect

Data concerning the consumption of wheat and wheat containing products were provided by the State Institute for Control of Agricultural Products (RIKILT), see Appendix 2.

2. Concentration limits of DON in (cleaned) wheat and in wheat containing food products

2.1 Concentration limit of DON in (cleaned) wheat

Based on a TDI of 1.1 μg DON per kg body weight and assuming a child with a high wheat consumption (8.5 g/kg body weight per day, which is the 95th percentile), the concentration limit of DON in wheat can be calculated according to:

Concentration limit of DON in (cleaned) wheat =
1.1 / 8.5 = 0.129 μg /g wheat = 129 μg/kg wheat (129 ppb)

2.1.1 Concentration limit of DON in wheat containing food products

The calculation of concentration limits of DON for wheat containing food products has been restricted to those wheat containing food products that substantially contribute to the total wheat consumption. Wheat containing food products with relatively high wheat contents were identified. The wheat intake of the total population as well as the wheat intake of children through these products were taken into account. The relative contribution of food product categories to the total wheat intake is shown in Table 1 (based on Kistemaker C. *et al*., 1998).

Table 1. Contribution of food categories to the total wheat intake (as %)

	Total population*	Boys (1-4 yr.)*	Girls (1-4 yr.)*
Bread	72	61	64
Breakfast cereals**	0.7	6.8	5.9
Cookies**	2.8	5.8	4.8
Pasta**	5.7	4.9	5.4

*) Data refer to the mean intake of the (sub)population
**) For these food categories only the wheat containing food products mentioned in Table 2 were considered

The product categories mentioned in Table 1 contribute for 81%, 79% and 80% to the total wheat consumption of the total population, boys and girls, respectively.

Based on the concentration limit of DON in (cleaned) wheat and the wheat content of the food product (Van Dooren, M.M.H. *et al.*, 1995), the concentration limits for wheat containing products were calculated (Table 2).

Table 2. Concentration limits of DON in wheat containing food products (based on a (cleaned) wheat concentration limit of 129 μg/kg)

NEVO Product code	product	% wheat	Concentration limit (μg/kg product)
230	Roll 'luxe witte'	61	79
233	Bread 'krenten'	41	53
236	Bread 'tarwe'	60	77
241	Bread 'wit-melk'	62	80
246	Bread 'volkoren'	60	77
248	Bread 'wit-water'	60	78
249	Bread 'mout tarvo'	60	77
878	Croissants 'bereid blik Danerolle'	64	82
1459	Bread 'krenten volkoren'	41	53
225	Brinta, Honig	100	129
1804, 9662	7 granen energieontbijt, Bambix groeiontbijt	30 *	39
9664	Bambix volkoren verrijkt	46	59
252	biscuit	98	127
258	cookies	39	51
261	speculaas	44	57
659	Pasta, cooked	31	45
811	Pasta, uncooked	100	129

*) assumption

Since the concentration limit of DON in a wheat containing food product depends on the wheat content, the number of concentration limits would equal the number of food products. To facilitate governmental surveillance and enforcement activities, general concentration limits are proposed for two food categories:

Bread : 60 μg/kg
Wheat containing food products (wheat content > 33%) : 120 μg/kg

The considered food products cover approximately 80% of the total wheat intake. Deriving concentration limits for governmental surveillance and enforcement activities for other wheat containing food products is considered ineffective (large variation in wheat content, large number of products). Therefore, it is suggested for food products with a wheat content < 33% to monitor the (cleaned) wheat used as an ingredient instead of monitoring the food product. To get in line with the general concentration limits of bread and other wheat products, we propose the concentration limit for

(cleaned) wheat : 120 μg/kg

instead of the 129 μg/kg calculated previously.

3. Daily DON intake of children

Children (1-4 yr.) are the population at risk concerning the exposure (relatively high wheat consumption) and the toxic effects of DON. Therefore, we calculated the hypothetical DON-intake based on the concentration limits of 60 and 120 μg/kg for bread and other wheat containing food products (wheat content > 33%), respectively, and on the intake of these food products (Kistemaker C. *et al*., 1998, see appendix 2). Assuming a body weight of 10 kg, the contribution of the DON intake is calculated and compared with the TDI. For boys consumption of wheat containing food products contaminated with DON at the concentration limits results in a DON intake of 106% of the TDI. For girls, the intake of DON through wheat containing food products amounts to 76% of the TDI. Please note, that the considered food categories contribute for 79% and 80% to the total wheat consumption for boys and girls, respectively.

Since it is very unlikely that all wheat containing products will contain the full maximum permitted concentrations simultaneously, it is concluded that the proposed limits will efectively keep the exposure levels below the TDI.

Table 3. Daily DON intake of children (1-4 yr.) assuming general concentration limits

Product	Intake (g/day), boys*	Intake (g/day), girls*	Conc. limit (μg/kg)	DON intake boys (μg)	DON intake girls (μg)
Bread	51	46	60	3.1	2.8
Breakfast cereals	41	23	120	4.9	2.8
Cookies	9	9	120	1.1	1.1
Pasta, uncooked**	22	14	120	2.6	1.7
Total DON (μg)				11.7	8.3
% TDI				106	76

*) Data refer to the mean consumption of children who actually consume the specific food products (indicated as ‘users’ in appendix 2, table 5). If a food category consisted of various wheat containing food products, the food product with the highest reported mean intake was selected. These may be considered as worst case assumptions, since a child may not be ‘user’ of all categories and may not consume as much as the highest mean intake reported for a wheat containing food product.
**) Cooked pasta contains approximately one third of the original wheat content (Table 2). The consumption of cooked pasta is 66 and 43 g per day for boys and girls, respectively (appendix 2). This corresponds to the consumption of 22 and 14 g uncooked pasta per day.

4. Discussion and Conclusions

4.1 Discussion

Considering children (1-4 yr.) as the population at risk, concentration limits for DON in (cleaned) wheat and wheat products have been calculated. Since we assumed that wheat forms the major source of DON-uptake in the Netherlands, possible DON-intake through cereal grains other than wheat has not been taken into account. If other cereal grains do contribute substantially to the DON-intake, the concentration limits of wheat and wheat containing food products should be adjusted.

Based on a provisional TDI of 1.1 μg/kg body weight and considering a child with a high wheat consumption (8.5 gram wheat per kg body weight per day), a concentration limit of 129 μg/kg wheat was derived. At this concentration limit no adverse health effects are expected for the general population and for children.
Depending on the wheat content of food products, concentration limits for DON can be derived for each food product. To facilitate governmental surveillance and enforcement activities, we propose the following general concentration limits:

(cleaned) wheat	:	120 μg/kg
Bread	:	60 μg/kg
Wheat containing food products (> 33% wheat)	:	120 μg/kg

For wheat containing food products with a wheat content of less than 33%, we suggest to only monitor the (cleaned) wheat (concentration limit 120 μg/kg).

Considering the general concentration limits and the consumption profile of children who actually use food products with a relatively high wheat content, the daily DON intake equals 76% (girls) and 106% (boys) of the provisional TDI if all products would contain DON at the proposed concentration limits. Since the considered food products contribute to approximately 80% of the total wheat intake, the total DON intake of children will probably not exceed the TDI. It should be noted that the consumption profile used for this calculation is rather worst case and will only be applicable to a limited number of children since a child (i) may not be 'user' of each food category, and (ii) if being a 'user' may consume to a lesser extent than is assumed.

In view of the current contamination levels of DON in (cleaned) wheat, the concentration limits mentioned above may be difficult to enforce. Therefore, higher concentration limits may be considered necessary or unavoidable. To derive the safe concentration limits mentioned above we assumed a child with a high (95^{th} percentile) wheat consumption. A lower percentile may be considered temporarily acceptable since the most relevant toxic effect (growth retardation) is considered to be a reversible effect.

If we assume a child with a median (50^{th} percentile) wheat consumption (i.e., 4.5 g wheat/kg body weight), the general concentration limits are two-fold higher:

(cleaned) wheat	:	240 μg/kg
Bread	:	120 μg/kg
Wheat containing food products (>33% wheat)	:	240 μg/kg

Based on these concentration limits the DON-intake of 'users' would amount to 151% and 213% of the provisional TDI (girls and boys, respectively). Please note that the considered wheat containing food products contribute to approximately 80% of the total wheat intake.

4.2 Conclusions

Considering children (1-4 yr.) as the population at risk for DON-exposure, the following concentration limits are proposed:

(cleaned) wheat	: 120 μg/kg
Bread	: 60 μg/kg
Wheat containing food products (>33% wheat)	: 120 μg/kg
Wheat containing food products (<33% wheat)	: monitor (cleaned) wheat only

At these concentration limits, adverse health effects are not expected for the general population and for children.

In view of the current contamination levels of DON in (cleaned) wheat, these concentration limits may be difficult to enforce. Considering growth retardation as a reversible toxic effect two-fold higher concentration limits may be considered temporarily acceptable.

Acknowledgements

The contributions of J.D. van Klaveren and M.M.H. van Dooren of the State Institute for Quality Control of Agricultural Products (RIKILT) are gratefully acknowledged.

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Appendix 1 Toxicology

A.J. Baars, M. van Apeldoorn, M. Wouters

Summary

Deoxynivalenol (DON, vomitoxin) is a trichothecene mycotoxin produced by *Fusarium* species, and prevalent world-wide in all sorts of cereal grains. Upon ingestion it can cause severe toxicosis in humans and farm animals. The main effect at low dietary concentrations is growth retardation and reduced food consumption, while higher doses induce vomiting. DON affects the immune system and alters various blood parameters; in addition it is a potential gastrointestinal irritant.
There are no indications for carcinogenic and/or mutagenic properties of DON. The evaluation for human risks can thus be based on a no-effect level from reported toxicity studies, applying an uncertainty factor. Considering the quality of the studies evaluated and the relevance of the toxicological endpoints, the chronic mouse study reported by Iverson *et al.* [1995] offers the most reliable data for a TDI estimation. The NOAEL in this study was 0.11 mg DON per kg body weight per day for reduction in weight gain as the end point. Applying an uncertainty factor of 100 results in a provisional TDI of 1.1 μg per kg body weight per day; this TDI is provisional because it is based on only one chronic toxicity study.

Introduction

Deoxynivalenol is a mycotoxin produced by fungi of the *Fusarium* genus, which are abundant in various cereal crops (wheat, maize, barley, oats, rye) and processed grains (malt, beer and bread). Chemically it belongs to trichothecenes: tetracyclic sesquiterpenes with a 12,13-epoxy group [cited in Eriksen & Alexander, 1998].

Chemical and physical data

4-Deoxynivalenol (DON; vomitoxin, dehydronivalenol, 4-deoxynivalenol, RD-toxin): 12,13-epoxy-3,4,15-trihydroxytrichotec-9-en-8-one (Fig. 1), $C_{15}H_{20}O_6$, MW: 296,32, CAS nr.: 51481-10-8.

DON is a white crystalline substance with a melting point of 151-153 °C. It is optically active and is soluble in ethanol, methanol, ethyl acetate, water and chloroform. The substance is a very stable compound, during both storage/milling and the processing/cooking of food, and does not degrade at high temperatures [cited in Rotter *et al.*, 1996; Ehling *et al.*, 1997].

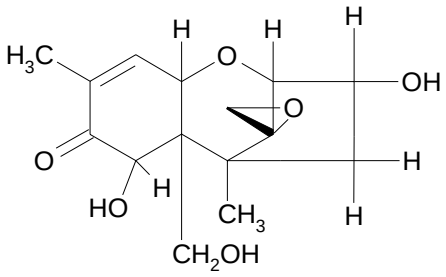

Fig. 1 Deoxynivalenol, structural formula

Biochemical mechanisms of actions

DON inhibits protein synthesis at the ribosomal level, and it has been demonstrated to inhibit DNA and RNA synthesis. The toxin has a haemolytic effect on erythrocytes. At low concentrations in the diet DON reduces growth, feed consumption (anorexia), whereas at higher acute doses it induces vomiting (emesis). Both effects, which are also seen with other trichothecene toxins, are thought to be mediated by affecting the serotoninergic activity in the CNS [Rotter *et al.*, 1996; Eriksen & Alexander, 1998].

Toxicokinetics

Ninety-six hours after administration of a single dose of radioactive-labelled DON (10 mg/kg body weight (bw)) to rats, 64 % of the radioactivity was recovered in the faeces and 25 % in the urine. After oral administration the main metabolite in faeces was de-epoxynivalenol. This metabolite was also found in faeces, urine, plasma and milk of lactating cows; in addition its presence was demonstrated after one week incubation with gut microflora from cows and swines, probably due to microbiological adaptation of the gut flora. In sheep and cows glucuronidation of DON was observed [cited in Eriksen & Alexander, 1998].

Toxicity

Acute and subacute toxicity

Oral LD_{50}-values of 78 and 46 mg/kg bw were reported for B6C3F1 and DDY mice, respectively [cited in Eriksen & Alexander, 1998; IARC, 1993]. For hens an oral LD_{50} of 140 mg/kg bw was reported [cited in IARC, 1993]. Signs of intoxication were vomiting, refusal of food, weight loss and diarrhoea [cited in Eriksen & Alexander, 1998].
The lowest oral dose for swines (bw 9-10 kg) resulting in vomiting varied between 50 and 200 μg/kg bw [cited in Eriksen & Alexander, 1998]. Swines are very sensitive to DON in the feed, and reduction of food uptake was seen at 1-2 mg DON per kg feed. Several studies indicated also changes in haematological parameters, but these effects could have been caused by the reduced food uptake [cited in Eriksen & Alexander, 1998].

Subchronic toxicity

Reduced food uptake of mice was reported at doses > 4-8 mg DON per kg feed; the same effect was noted in rats at 12-20 mg/kg feed [cited in Rotter *et al.*, 1996].
In a 5-week study with mice a no-effect level of 0.25 mg/kg bw/day was observed; at 0.5 mg/kg bw/day a reduction of the α_1 and α_2 globulin levels was seen [cited in Eriksen & Alexander, 1998].
A 9-week diet study with rats showed at all dosages (= 0.25 mg/kg bw/day) a reduction of both weight gain and food uptake [Arnold *et al.*, 1986].
In a 90-days study with rats a dose of 20 mg DON per kg feed (equivalent to 1 mg/kg bw/day) resulted in reduced weight gain, but effects on serum enzyme levels or haematological parameters were not observed. Histopathological changes were not noted [Morrissey *et al.*, 1985].
In a 28-days study with swines (7 animals per group, age 6-7 weeks, mean bw 13.3 kg) the animals received 0, 0.75, 1.5 or 3.0 mg DON per kg feed (as contaminated corn), equivalent to 0, 0.03, 0.06 or 0.12 mg/kg bw/day. The food contained also 15-acetyl-DON (approximately 20 % of the DON-content). In all experimental groups food uptake was reduced. A dose-related decrease of skin temperature was noted during the first 7 days. Absolute and relative thyroid weights were decreased. Increased T4-levels, increased serum albumin and serum albumin/globulin ratio, and decreased α-globulin values were observed. Treated animals had a delayed response and a lower antibody titre following immunisation with sheep RBCs. Macroscopically corrugation of the fundic region of the stomach was observed. [Rotter *et al.*, 1994].
In a 42-days swine study (8 swines per group, bw 18.0-50.8 kg) the animals were administered 0 or 4 mg DON per kg feed (as contaminated corn), equivalent to 0 or 0.15 mg/kg bw/day. A 20 % reduction of food uptake and a 13 % reduction of weight gain were observed. Organ weights were normal. Also in this study corrugation of the stomach was seen. In weeks 2 and 3 decreased serum-protein levels, and in weeks 2 and 4 decreased β-globulin values were noted. These values were normal at the end of the study [Rotter *et al.*, 1995].

In a third study swines (7-12 males and 8-14 females per group, bw approximately 25 kg) received 0, 0.5, 1.0, 2.0 or 4.0 mg DON per kg feed (as contaminated oats) during 85-100 days. These dosages were equivalent to 0, 0.02, 0.04, 0.08 or 0.16 mg/kg bw/day. At 2 and 4 mg/kg feed a dose-related reduction of weight gain was observed. At 4 mg/kg feed also a reduced food uptake and food conversion were reported. These changes were not noted at 0.5 and 1.0 mg/kg feed. DON had no effect on IgA activity [Bergsjø *et al.*, 1992].
In a fourth swine study (age ca. 60 days, bw 21-22 kg, 7-9 males and 10-11 females per group) the animals were given 0, 0.7, 1.7 or 3.5 mg DON per kg feed (as contaminated oats) during 94-96 days. These dosages were equivalent to 0, 0.025, 0.06 or 0.12 mg/kg bw/day. At 3.5 mg/kg feed, reduced food uptake and reduced weight gain, increased liver weights, decreased serum-protein and serum-albumin levels, and temporary decreases in PCV, serum-calcium and serum-phosphorus levels were observed. A reduced food uptake was also noted at 1.7 mg/kg feed. Significant effects on other parameters (skeleton quality, IgA activity, other haematological parameters, histopathology of livers, kidneys, pancreas, Peyer's patches, and mesenteric lymph nodes) were not observed [Bergsjø *et al.*, 1993].

Chronic toxicity and carcinogenicity

In a chronic diet study with B6C3F1 mice the animals were administered 0, 1, 5 or 10 mg DON per kg feed, daily during 2 years (males: 0, 0.1, 0.5 or 1.1, females: 0, 0.1, 0.7 or 1.5 mg/kg bw/day). Corn oil (4 %) was added to the DON-containing feed to prevent environmental contamination with DON-containing dust. Survival was not significantly changed. A significantly reduced weight gain was seen in males and females at 5 and 10 mg/kg feed. DON did not cause biologically relevant effects in haematological and clinical-chemical parameters. In females serum immunoglobulines showed some increase of IgA and IgG (< 10%) at 5 and 10 mg/kg feed. Relative liver weights in males were increased at 5 and 10 mg/kg feed; at 10 mg/kg feed also the relative testes weights were significantly increased. At this latter dosage males showed decreased relative spleen weights. No increased incidence of preneoplastic or neoplastic changes were observed. The no-effect level in this study is 1 mg/kg feed, corresponding with 0.11 mg/kg bw/day [Iverson *et al.*, 1995].
In a two-stage experiment with Sencar mice, DON did not show any characteristics of skin tumour initiation or promotion [Lambert *et al.*, 1995].
The IARC classified DON in 1993 in Category 3, i.e., not classifiable as to its carcinogenicity to humans. In 1993, however, the negative chronic study in mice [Iverson *et al.*, 1995] was not available.

Mutagenicity

DON did not show mutagenic activity in Ames tests with *Salmonella typhimurium*. both with and without S-9 activation systems, and in an *in vitro* UDS test using rat primary hepatocytes. DON induced cell transformation in mouse embryo cells in vitro,

and induced clastogenic effects and inhibited gap-junctional intercellular communication in Chinese hamster V79 cells, but these effects may be secondary to inhibited protein synthesis and cytotoxic effects (cited in Erikson & Alexander, 1998]. The IARC [1993] concluded that DON induces cell transformation, chromosomal aberrations, and inhibits gap-junctional intercellular communication in cultered mammalian cells, but that it does not induce mutations in bacteria or UDS in mammalian cells.

Immunotoxicity

Studies with experimental animals demonstrated effects on the immune system, notably effects on IgA. There are indications for a suppression of humoral and cellular immunity, resulting in an increased susceptibility for infectious diseases, as shown in studies with mice [cited in Eriksen & Alexander, 1998; Deijns *et al.*, 1994]. Regarding this increased susceptibility for infectious diseases a no-effect level of 0.25 mg/kg bw/day [Tryphonas *et al.*, 1986] and a lowest-effect level of 0.22 mg/kg bw/day have been reported in studies with male Swiss-Webster and male Balb/C mice, respectively [cited in Eriksen & Alexander, 1998; Deijns *et al.*, 1994]. Perinatal investigations with respect to the immune system are not available.

Reproduction toxicity and teratogenicity

Swiss-Webster mice (15-19 per group) were daily administered (gavage) 0, 0.5, 1.0, 2.5, 5, 10 or 15 mg DON per kg bw, during days 8-11 of pregnancy. On day 19 of pregnancy the dams were killed (CO_2) [Khera *et al.*, 1982]. Dams showed a dose-related reduction of body weight at doses = 5 mg/kg bw/day. Doses = 10 mg/kg bw/day resulted in resorption of all embryos, at 5 mg/kg bw/day 80 % embryonal resorption was observed, while also in the 2.5 mg/kg bw/day dose group a significant increase of the number of resorptions was noted. Skeletal abnormalities (vertebrae, ribs, sternebrae) were dose-relatedly present in the 1 - 5 mg/kg bw/day dose groups. Histologically no DON-related pathological changes were seen. The LOAEL (lowest observed adverse effect level) and NOAEL (no observed adverse effect level) in this study were established at 1.0 and 0.5 mg DON per kg bw per day, respectively.
Pregnant rabbits (New Zealand White, 13-15 animals per group) received daily 0, 0.3, 0.6, 1.0, 1.6, 1.8 or 2.0 mg DON per kg bw via the feed during days 0-30 of pregnancy [Khera *et al.*, 1986]. In the 1.0 and 1.6 mg/kg bw/day dose groups a decreased foetal weight was observed. Complete foetal resorption occurred at 1.8 and 2.0 mg/kg bw/day. Dosages not resulting in maternal toxicity (0.3 and 0.6 mg/kg bw/day) did not evoke abnormalities in foetuses *à terme*. Teratogenic effects were not observed. The NOAEL in this study was 0.6 mg/kg bw/day.
Weaned Swiss-Webster F_0 mice received 0.375, 0.75 or 1.5 mg DON per kg bw per day (7 males, 59 females) or 2.0 mg DON per kg bw per day (15 males, 15 females) via the feed. After 30 days the animals were paired and the F_{1a} offspring was observed during 3 weeks. The F_0 dams were paired again, and at day 19 of pregnancy the F_{1b} foetuses were checked with regard to anatomical abnormalities [Khera *et al.*, 1984]. After one week of administration of 2 mg DON per kg bw per day the F_0 animals

showed permanently decreased body weights, and after 3 weeks the food uptake was significantly and permanently decreased. In this dose group postnatal survival and body weights of the F_{1a} pups were significantly changed: during the 3 weeks observation period the mortality of control pups increased from virtually 0 to 20 %, while after one week the mortality in the treated group was already 90 %. The surviving pups did not show macroscopical of histological abnormalities. The second mating of the F_0 animals of the 2 mg/kg bw/day dose group resulted in a higher incidence of embryonal resorptions, a smaller number of live foetuses, and a decreased mean foetal weight. External and visceral malformations were not significantly different from controls; skeleton abnormalities, however (related to the reduced foetal weight), were observed. In the 1.5 mg/kg bw/day dose group food and water consumption of the F_0 animals was temporary decreased, but this did not result in significantly decreasing body weights. After the second mating of the F_0 animals changes of the reproduction parameters were not observed. In the 0.75 and 1.5 mg/kg bw/day dosage groups the mortality of the F_{1b} pups was increased. On termination of the experiment the dams did not show macroscopical or histopathological abnormalities. In the F_{1b} pups no teratogenic effects were observed. The study authors did not conclude to a NOAEL, but from their critical evaluation of the observed effects a LOAEL of 1.5-2.0 mg/kg bw/day can be deducted, which results in a NOAEL of 0.375 mg/kg bw/day.

Sprague-Dawley rats (15 males and 15 females per group) were given 0.25, 0.5 or 1.0 mg DON per kg bw per day via the feed, from 6 weeks before up to and including pregnancy. The animals were killed at day 22 of pregnancy, and the foetuses were checked with respect to viability, body weight, and presence of macroscopical, visceral and skeletal abnormalities [Khera *et al.*, 1984]. Maternal toxicity was not observed, and neither the males nor the females showed abnormalities of the reproduction parameters or reproduction organs. Foetal anatomy did not differ from controls, except for a significant and dose-related increase of renal pelvis and urinary bladder dilatation in all dosage groups. The study authors considered this finding irrelevant and did not conclude to a LOAEL or NOAEL. Thus, from this study a NOAEL of = 1 mg/kg bw/day can be deducted.

Sprague-Dawley rats (25 males and 25 females per group) received feed containing DON at a level of 20 mg/kg (equivalent to ca. 2 mg/kg bw/day) before mating (males 60 days, females 15 days) and during pregnancy [Morrissey & Vesonder, 1985]. In dams of the treated group a decreased body weight was found, together with some decrease in fertility (in the treated group 50 %, and in the control group 80 % of the matings resulted in pregnancy). Histological abnormalities of testes and ovaries were not observed. The decreased fertility in this study indicates a LOAEL of = 2 mg/kg bw/day.

Eriksen & Alexander [1998] evaluated two studies in swines, in which the animals were exposed to DON during pregnancy. In the first study the animals were killed at day 50-54 of pregnancy, the other study observed the animals up to three weeks lactation. Gilts were given feed containing 0.1-4.8 DON per kg. These doses did not result in maternal toxicity or decreased food consumption, but doses = 1-2 mg/kg resulted in a decreased weight gain. Effects regarding number of newborns, survival or malformations were not observed. In doses smaller than the ones at which decreasing weight gain was observed, effects of DON on reproduction parameters

were not seen. The LOAEL (maternal toxicity) in this study was 1-2 mg DON per kg food, equivalent to 0.03-0.07 mg/kg bw/day.

Effects in humans

Erikson & Alexander [1998] cite some epidemiological studies in which cases of food poisoning by contaminated grains are discussed. The symptoms described include abdominal pain or a feeling of fullness in the abdomen, dizziness, headache, throat irritation, nausea, vomiting, diarrhoea, and blood in the stool. These were all reversible effects.
In one of these studies, reporting human food poisoning caused by infected wheat in India in 1989 which affected an estimated 50,000 people, a NOAEL of 0.44 μg/kg bw was calculated, using an average intake of 67 g wheat products and a mean bw of 52 kg. However, samples were collected four months after the outbreak, and the exposure was not limited to DON but included also other toxins, which leads to gross uncertainties in the estimated NOAEL.

Evaluation

Generally the toxic effects of DON are reversible (except of course after acute administration of high doses). There are no indications for DON having carcinogenic and/or mutagenic properties. Thus, the evaluation for human risks can be based on a no-effect level from toxicity studies, applying an uncertainty factor. The NOAELs and LOAELs reported for DON vary between 0.04 - 0.75 mg/kg bw/day and are summarised in Table 1.
Taking into account the quality of the studies evaluated and the relevance of the toxicological endpoints, the following NOAELs are to be considered:

Study	NOAEL (mg/kg bw/day)	Reference
Mouse, chronic (2 years)	0.11	Iverson *et al.*, 1995
Mouse, immunotoxicity	0.25	Tryphonas *et al.*, 1986
Mouse,teratogenicity	0.5	Khera *et al.*, 1982
Mouse, reproduction toxicity	0.375	Khera *et al.*, 1984
Swine, subchronic (90-95 days)	0.04-0.06	Bergsjø *et al.*, 1992, 1993

Extrapolation from experimental animals to humans implies the application of an uncertainty factor (UF). Commonly a UF of 10 is used for extrapolating from rodents to humans, and an additional UF of 10 to cover for (human) interindividual differences. In the case of swine these UFs are 2 and 10, respectively. For the data above this would result in tolerable daily intakes which are all in the same order of magnitude (i.e., 1.1-5.0 μg/kg bw/day).

Conclusion

Considering that:
(1) the lowest TDI is the one derived from the chronic mouse study (in which the most important consideration is the fact that this is a chronic study of good quality), and -
(2) although the swine might be more resembling humans with regard to its physiology, in the studies evaluated the quality of the DON preparation used was not 100 %, -
it is decided to use the NOAEL of the chronic diet study with mice (0.11 mg/kg bw/day) for the estimation of a provisional TDI. Applying an uncertainty factor of 100 as outlined above, a provisional TDI of 1.1 μg/kg bw/day is estimated, in line with Ehling *et al.* [1997], and Eriksen & Alexander [1998]. This TDI is provisional because chronic toxicity has only been studied in one animal species.

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Table 1 **Deoxynivalenol: NOAELs and LOAELs**

Species	**Study**	**Effect**	**Parameter**	**Dose *)**	**Reference**
Mouse	Acute	Mortality	LD_{50} oral	46-78	Eriksen & Alexander, 1998
Hen	Acute	Mortality	LD_{50} oral	140	IARC, 1993
Swine	Acute	Vomiting	-	0.05-0.2	Eriksen & Alexander, 1998
Swine	Subacute	reduced food uptake	-	0.03-0.07 (1-2 mg/kg feed)	Eriksen & Alexander, 1998
Mouse	Subacute	reduced food uptake	-	0.6-1.2 (4-8 mg/kg feed)	Rotter *et al.*, 1996
Rat	Subacute	reduced food uptake	-	0.75-1.0 (15-20 mg/kg feed)	Rotter *et al.*, 1996
Mouse	5 weeks	decreased α1/α2 globulin ratio	NOAEL	0.25	Eriksen & Alexander, 1998
Rat	9 weeks	reduced growth, reduced food uptake	LOAEL	0.25	Arnold *et al.*, 1986
Rat	90 days	reduced growth	LOAEL	1.0	Morrissey *et al.*, 1985
Mouse	2 years	reduced growth	NOAEL	0.11	Iverson *et al.*, 1995
Mouse	Immunotoxicity	increased susceptibility for infections	NOAEL	0.25	Tryphonas *et al.*, 1986
Mouse	Immunotoxicity	increased susceptibility for infections	LOAEL	0,22	Deijns *et al.*, 1994
Mouse	Teratogenicity	foetal skeleton abnormalities	NOAEL	0.5	Khera *et al.*, 1982
Mouse	Reproduction-toxicity	mortality of pups	NOAEL	0.375	Khera *et al.*, 1984
Rat	Reproduction-toxicity	maternal and/or embryotoxicity	NOAEL	= 1.0	Khera *et al.*, 1984
Rat	Reproduction-toxicity	reduced fertility	LOAEL	≤ 2.0	Morrissey & Vesonder, 1985
Rabbit	Teratogenicity	reduced foetal weight	NOAEL	0.6	Khera *et al.*, 1986
Swine	Reproduction-toxicity	reduced growth (maternal toxicity)	LOAEL	0.03-0.07 (1-2 mg/kg feed)	Eriksen & Alexander, 1998
Swine	28 days	reduced food uptake, decreased thyroid weight and α-glob., increased T4, serum-albumin and A/G ratio	LOAEL	0.03 (0,75 mg/kg feed)	Rotter *et al.*, 1994
Swine	42 days	reduced growth, reduced food uptake, stomach corrugation	LOAEL	≤ 0.15 (= 4 mg/kg feed)	Rotter *et al.*, 1995
Swine	90 days	reduced growth, reduced food uptake	NOAEL	0.04 (1 mg/kg feed)	Bergsjø *et al.*, 1992
Swine	95 days	reduced growth, reduced food uptake, increased liver weight, decreased serum albumin	NOAEL	0.06 (1.7 mg/kg feed)	Bergsjø *et al.*, 1993

*) All dosages in mg/kg bw/day, unless indicated otherwise.

Appendix 2

Overview of the total wheat consumption of the Dutch population and the contribution of wheat containing food products to that consumption

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5. *RIKILT

Summary

This appendix provides the background data used to calculate the concentration limits of DON in (cleaned) wheat and wheat containing food products. The data concern the consumption of primary agricultural products in the Netherlands, the consumption of food products (national food consumption survey), the distribution of the wheat consumption in the Dutch population and the contribution of wheat containing food products to the total wheat consumption.

Consumption of primary agricultural products

In the Netherlands consumer food is coded and described (nutrients, energy content) in the Dutch Nutrient Data base (NEVO). In the Conversion model Primary Agricultural Products (CPAP), developed by the State Institute for Quality Control of Agricultural Products (RIKILT), each NEVO-coded food product is described in terms of primary agricultural products. With this model it is possible to convert food consumption survey data into the amount of primary agricultural products consumed by the population under research (Van Dooren *et al.*, 1995).

In the Netherlands wheat is applied in a large number of food products, mostly in the form of (wholemeal) wheat flour, flour and starch. In about 22% of the food products coded in the NEVO-table the ingredient wheat has been processed. Wheat containing food products vary from wheat bread, pasta (macaroni), breakfast cereals, spiced biscuits (‘speculaas’) to packages of soup. The wheat content of these food products ranges from 1% to 100%.

Consumption data

Data on the food consumption pattern of individuals was obtained by the Dutch National Food Consumption Survey (VCP). In 1997/1998 this survey was performed for the third time and contains data of 5958 persons ranging from 1 to 75 years of age (Kistemaker *et al*., 1998). The survey includes a description of the daily consumption over two consecutive days and a recording of age, sex and body weight (bw) for each individual. By means of the CPAP the consumption data of the several VCP-food products were transformed to wheat consumption data (in g/day and in g/kg bw/day).

Wheat consumption in the Dutch population

In the Netherlands the average wheat intake per day due to the consumption of wheat containing products, is 111 g (Table 1). For an average person this corresponds with a wheat consumption of 2.0 g/kg bw/day. In general, the wheat intake of boys and men is higher than the intake of girls and women (2.1 g/day and 1.8 g/day, respectively). Children aged 1 to 4 have the highest wheat intake, i.e., 4.5 – 8.5 g/kg bw/day.

Table 1. Distribution of the wheat consumption in the Dutch population

		g/day				g/kg bw/day			
Population	N	Mean	Std	Median	95%	Mean	Std	Median	95%
DNFCS-1997-98 POPULATION	5958	111	51	105	204	2.0	1.2	1.7	4.3
MEN	2789	127	57	121	227	2.1	1.3	1.8	4.6
WOMEN	3169	97	41	94	167	1.8	1.1	1.6	3.9
BOYS, 1-4 YEAR	135	63	25	63	101	4.5	1.8	4.3	7.3
GIRLS, 1-4 YEAR	119	58	23	53	103	4.5	1.8	4.0	8.5
BOYS, 4-7 YEAR	138	81	29	78	131	4.1	1.4	3.9	6.4
GIRLS, 4-7 YEAR	138	73	25	69	117	3.7	1.3	3.4	6.9
BOYS, 7-10 YEAR	104	98	32	95	159	3.4	1.1	3.3	5.4
GIRLS, 7-10 YEAR	134	85	29	78	143	3.0	1.1	2.8	4.9
BOYS, 10-13 YEAR	112	116	39	112	182	3.0	1.1	2.8	4.9
GIRLS, 10-13 YEAR	124	104	34	103	158	2.6	1.0	2.7	4.1
BOYS, 13-16 YEAR	137	134	50	133	220	2.5	1.0	2.4	4.2
GIRLS, 13-16 YEAR	117	106	35	105	166	2.0	.8	2.0	3.4
MEN, 16-19 YEAR	142	148	56	149	235	2.2	.9	2.2	3.6
WOMEN, 16-19 YEAR	139	111	41	108	182	1.9	.7	1.8	3.2
MEN, 19-22 YEAR	130	143	62	137	252	1.9	.8	1.9	3.3
WOMEN, 19-22 YEAR	128	104	41	101	177	1.6	.7	1.6	3.1
MEN, 22-50 YEAR	1252	142	58	136	243	1.8	.8	1.7	3.1
WOMEN, 22-50 YR, NOT PREGNANT	1472	104	42	101	177	1.5	.7	1.5	2.8
MEN, 50-65 YEAR	454	125	52	122	219	1.6	.7	1.5	2.8
WOMEN, 50-65 YEAR	512	91	39	86	158	1.3	.6	1.2	2.3
MEN, 65+ YEAR	185	105	44	101	179	1.4	.6	1.3	2.4
WOMEN, 65+ YEAR	236	88	34	83	144	1.2	.5	1.2	2.2
PREGNANT WOMEN	50	106	47	112	167	1.7	.8	1.5	3.0
VEGET., VEGANISTS, MACROBIOTS, ANTROP.	69	106	47	104	187	1.7	.8	1.5	3.0
VEGETARIANS	62	106	48	96	187	1.7	.8	1.5	3.0

Contribution of wheat containing food products to the total consumption of wheat

The contribution of wheat containing food products to the total wheat consumption has been established. By this, the main sources of wheat consumption can be determined. Table 2 presents the consumption of food products with a high wheat content (>67%). In Table 3 the consumption of food products with a moderate wheat content (33 – 67%) is presented. The only product with a lower wheat content (31.1%) which contributed significantly (5.7%) to the total wheat intake was cooked pasta (macaroni). In Table 4 the contribution of food categories to the mean consumption of wheat is presented. Bread is the main source of wheat intake in the total Dutch population (accounts for 72% of the total consumption of wheat).

Children (aged 1 - 4 yr.) are the population group at risk concerning the exposure (relatively high wheat consumption) and the toxic effects of DON. In this age group, the food category of breakfast cereals is a relative important contributor to the total wheat intake, next to bread [Kistemaker et al., 1998]. To calculate the possible DON-intake in children, the mean consumption of children who actually ‘use’ (‘users’ consumed the product during the food survey) specific food products is used. In Table 5 the mean (wheat) consumption of ‘users’ (1 – 4 yr.) of food products which highly contribute to the total wheat intake is presented.

Table 2. Wheat content (%), mean food consumption (g/day) and mean wheat consumption (g/day) for food products with a high wheat content (> 67%)

NEVO_code	food product	% wheat	*DNFCS-1997/1998 population* [1]		*Boys 1 - 4 yr* [2]		*Girls 1 – 4 yr* [2]	
			cons NEVO (g/day)	cons wheat (g/day)	cons NEVO (g/day)	cons wheat (g/day)	cons NEVO (g/day)	cons wheat (g/day)
252	Biscuit	98.3	1.08	1.1	2	2.0	2	2.0
227	Beschuit pak	86.1	1.18	1.0	1	0.9	1	0.9
1013	Paneermeel pak	90.0	0.88	0.8	1	0.9	0	0.0
225	Ontbijtprodukt pak Brinta Honig	100.0	0.75	0.8	2	2.0	1	1.0
220	Bloem tarwe- patent pak/zak	100.0	0.58	0.6	0	0.0	0	0.0
565	Brood geroosterd toast pak	86.7	0.54	0.5	1	0.9	0	0.0
811	Macaroni volkoren onbereid pak	100.0	0.47	0.5	0	0.0	1	1.0
263	Biscuit volkoren-	81.7	0.55	0.5	0	0.0	1	0.8
228	Cracker cream- pak	85.5	0.49	0.4	1	0.9	0	0.0
655	Beschuit volkoren pak	88.0	0.41	0.4	0	0.0	0	0.0
975	Knäckebröt sesam	79.0	0.31	0.2	0	0.0	0	0.0
1312	Toast naturel Cracottes pak	94.7	0.20	0.2	0	0.0	-	-
267	Stokjes zoute	94.0	0.19	0.2	0	0.0	0	0.0
78	Meel gries- poeder pak/zak	100.0	0.15	0.2	-	-	-	-
82	Vermicelli onbereid pak	114.5	0.11	0.1	-	-	0	0.0
596	Knäckebröt goudbruin	80.6	0.13	0.1	0	0.0	-	-
229	Knäckebröt gemiddeld	79.9	0.13	0.1	-	-	0	0.0
238	Cracker tea- matses pak	85.5	0.04	0.0	0	0.0	0	0.0
1802	Knäckebröt sandwich	71.0	0.05	0.0	-	-	-	-
590	Zemelen tarwe- pak	100.0	0.04	0.0	-	-	-	-
1015	Tarwe gebroken bulgur gedroogd pak	100.0	0.03	0.0	-	-	-	-
1020	Meel bak- zelfrijzend pak	100.0	0.03	0.0	-	-	0	0.0
1778	Knäckebröt maanzaad	103.9	0.03	0.0	-	-	-	-
222	Meel tarwe- pak/zak	100.0	0.02	0.0	-	-	-	-
1322	Cracker volkoren Cracottes pak	89.4	0.02	0.0	-	-	-	-
245	Voedingsbiscuit Sanovite	85.0	0.02	0.0	-	-	-	-
9611	Ontbijtproduct All Bran Kellogg's	85.0	0.02	0.0	-	-	-	-
1458	Seitan	100.0	0.02	0.0	-	-	-	-
992	Puddingpoeder griesmeel z suiker pak	110.5	0.01	0.0	-	-	-	-
518	Biscuit volkoren- goudgraantje	87.1	0.01	0.0	-	-	-	-
756	Biscuit ontbijt-	100.0	0.01	0.0	-	-	-	-
231	Kiemen tarwe- pak	100.0	0.01	0.0	-	-	-	-
1806	Ontbijtprodukt tarwebloem instant	100.0	0.01	0.0	0	0.0	-	-
1350	Bakmix wit glutenvrij Glutafin	71.0	0.01	0.0	1	0.7	-	-
1766	Kinderbiscuit Bambix	77.0	0.00	0.0	0	0.0	0	0.0
1805	Ontbijtprodukt tarwegries met honing	100.0	0.00	0.0	1	1.0	-	-
1765	Voedingsbiscuit start- Bambix	73.0	0.00	0.0	0	0.0	-	-
			8.5	7.8	10	9.3	6	5.7

% wheat > 100% can be explained by the higher dry material content of the food product compared to wheat flour

[1] data from RIKILT

[2] data from Kistemaker *et al.* (1998): consumption is rounded off to whole grams, therefore consumption of 0 g/day equals < 0,5 g/day

Table 3. Wheat content (%), mean food consumption (g/day) and mean wheat consumption (g/day) for food products with a moderate wheat content (33-67%)

			DNFCS-1997-98 population [1]		*Boys 1- 4 yrs* [2]		*Girls 1 – 4 yrs* [2]	
nevo_code	foodproduct	%_wheat	cons NEVO (g/day)	cons wheat (g/day)	cons NEVO (g/day)	cons wheat (g/day)	cons NEVO (g/day)	cons wheat (g/day)
236	Brood tarwe-	60.0	48.52	29.11	28	16.8	27	16.2
246	Brood volkoren-	60.0	32.86	19.70	16	9.6	15	9.0
248	Brood wit- water	60.1	27.41	16.48	12	7.2	12	7.2
230	Broodje luxe witte	60.9	8.20	4.99	3	1.8	2	1.2
241	Brood wit- melk	61.8	3.62	2.24	1	0.6	2	1.2
233	Brood krente-	40.8	4.60	1.88	5	2.0	3	1.2
470	Bami goreng zonder ei	42.0	3.02	1.27	1	0.4	1	0.4
261	Speculaas	43.9	2.32	1.02	2	0.9	1	0.4
878	Croissants bereid blik	63.9	1.31	0.83	1	0.6	1	0.5
258	Koekje	39.4	2.07	0.81	2	0.8	1	0.4
274	Creamer koffie- Completa	55.0	0.99	0.55	-	-	-	-
249	Brood mout-	60.0	0.86	0.52	0	0.0	0	0.0
530	Meel pannekoek- pak	50.0	0.95	0.47	1	0.5	1	0.5
1471	Biscuit chocolade-	49.2	0.79	0.39	1	0.5	0	0.0
265	Korstgebak zout	44.0	0.84	0.37	-	-	-	-
480	Chocoprince	37.3	0.86	0.32	0	0.0	0	0.0
1361	Brood wit- Turks	60.1	0.51	0.31	-	-	-	-
262	Spritsstukken	41.6	0.67	0.28	1	0.4	1	0.4
269	Kroepoek bereid	62.0	0.40	0.25	0	0.0	0	0.0
836	Taart zand-	49.4	0.43	0.21	0	0.0	0	0.0
1459	Brood krente- volkoren	40.8	0.51	0.21	0	0.0	1	0.4
789	Koek boter-	34.8	0.59	0.20	0	0.0	0	0.0
1478	Vlaai kruimel- gem	35.2	0.42	0.15	0	0.0	-	-
232	Broodje koffie-	39.9	0.35	0.14	-	-	-	-
531	Meel poffertjesmix pak	50.0	0.27	0.14	0	0.0	0	0.0
244	Brood rozijnen-	40.8	0.33	0.13	-	-	0	0.0
873	Voedingsbiscuit Evergreen krenten	63.9	0.20	0.13	0	0.0	0	0.0
474	Oliebol bereid in sojaolie	36.9	0.33	0.12	-	-	0	0.0
1319	Voedingsbiscuit Switch overige smaken	48.7	0.24	0.12	0	0.0	-	-
635	Krakeling	40.8	0.28	0.11	0	0.0	0	0.0
264	Biscuit zoute	54.0	0.19	0.10	0	0.0	0	0.0
1699	Koekje kaas- gemiddeld	46.0	0.20	0.09	0	0.0	0	0.0
481	Koek Bastogne	43.4	0.18	0.08	0	0.0	0	0.0
260	Lange vingers	40.8	0.12	0.05	1	0.4	1	0.4
235	Voedingsbiscuit kleuter	64.5	0.08	0.05	0	0.0	1	0.5
9664	Ontbijtprodukt volkoren Bambix V	46.0	0.08	0.04	1	0.5	2	0.9
899	Pasteibakje	54.0	0.06	0.03	0	0.0	-	-
898	Pasteibakje roomboter	65.1	0.05	0.03	-	-	-	-
1365	Baklava noten-honing gebak Turks	44.3	0.07	0.03	-	-	-	-
9612	Ontbijtproduct Fruit & Fiber Kellogg’s	55.0	0.06	0.03	-	-	-	-
234	Voedingsbiscuit peuter	60.8	0.04	0.03	0	0.0	0	0.0
554	Creamer koffie- pot	58.5	0.04	0.03	-	-	-	-
9655	Ontbijtproduct 8 granen appel-honing	43.0	0.04	0.02	0	0.0	0	0.0
9609	Ontbijtproduct Smacks Kellogg’s	52.0	0.03	0.02	-	-	-	-
1351	Bakmix bruin glutenvrij Glutafin	52.0	0.02	0.01	-	-	-	-
1339	Koekjes bere- Bambix	65.3	0.01	0.01	0	0.0	0	0.0
9663	Ontbijtprodukt gemengde granen Nutrix V	43.0	0.01	0.01	-	-	0	0.0
1355	Ontbijtprodukt volkoren Nutrigran	45.0	0.01	0.00	0	0.0	-	-
1780	Knäckebröt muesli	56.1	0.01	0.00	-	-	-	-
1711	Koekjes kinder- Circusvriendjes aardbei/	61.0	0.00	0.00	0	0.0	-	-
1477	Koekje voor diabetici	39.4	0.00	0.00	-	-	-	-
sum			146.06	84.10	76	43.0	72	40.8
1804	Ontbijtprodukt 7 granen energieontbijt[3]	30.0	0	0.0	1	0.3	1	0.3
9662	Bambix, volkoren verrijkt[3]	30.0	0	0.0	5	1.5	4	1.2

[1] data from RIKILT.
[2] data from Kistemaker *et al.* (1998): consumption is rounded off to whole grams, therefore consumption of 0 g/day equals < 0,5 g/day.
[3] these two breakfast cereals have a wheat content below 33%. However, in children (1-4 yr), the consumption of these products appeared to relatively high (Kistemaker *et al.*, 1998). These products are therefore also considered in the food category of breakfast cereals. The wheat content is estimated at approximately 30%, which is slightly lower but in the range of similar food products with a wheat content >33%.

Table 4. Relative contribution of food categories to the mean wheat consumption in the Netherlands

Food Categories	Relative contribution (%)
Bread	72
Grainproducts and binding agents	9
Pastry and cookies	9
Composed dishes	4
Snacks	3
Soup	1
Other	2

Table 5. Mean consumption of wheat containing food products and associated wheat consumption (g/day) per food product for children (1- 4 year) who actually consume these food products (‘users’). Only wheat containing food products which highly contribute to the total wheat intake are considered.

Food Categories (% wheat content)	Boys 1-4 yr.		Girls 1-4 yr.	
	Cons NEVO	Cons wheat	Cons NEVO	Cons wheat
Bread				
Broodje, luxe witte (60.9)	25	15.2	23	14.0
Brood, krente (40.8)	34	13.9	30	12.2
Brood, tarwe (60.0)	51	30.6	45	27.0
Brood, wil-melk (61.8)	32	19.8	33	20.4
Brood, volkoren (60.0)	51	30.6	46	27.6
Brood, wit water (60.1)	35	21.0	42	25.2
Brood, mout tarvo (60.0)	22	13.2	28	16.8
Croissants, blik (63.9)	20	12.8	20	12.8
Brood, krente volkoren (40.8)	13	5.3	22	9.0
Breakfast cereals				
Ontbijtprodukt pak Brinta, Honig (100)	27	8.0	22	22.0
Ontbijtprodukt, 7 granen energie (30*)	41	0.9	23	6.9
Bambix groeiontbijt, verrijkt (30*)	25	5.7	20	6.0
Bambix groeiontbijt, volkoren Verrijkt (46.0)	22	10.1	22	10.1
Pastry and cookies (98.3)				
Biscuit (39.4)	6	5.9	6	5.9
Koekjes (39.4)	8	3.2	9	3.5
Speculaas (43.9)	9	4.0	9	4.0
Other				
Macaroni, cooked (31.1)	66	20.5	43	13.4

* assumption

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