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Wang, X, Qiu, N, Zhang, C et al. (4 more authors) (2021) Comprehensive dietary and internal exposure assessment of deoxynivalenol contamination in a high-risk area in China using duplicate diet studies and urinary biomarkers. Food Control, 124. 107830. p. 107830. ISSN 0956-7135

https://doi.org/10.1016/j.foodcont.2020.107830

Comprehensive dietary and internal exposure assessment of deoxynivalenol contamination in a Chinese population using duplicate diet studies and urinary biomarkers

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Abstract

This study assessed the exposure of a considerably large Chinese population sample from the Anhui Province, China, to deoxynivalenol (DON) based on their dietary intake and urinary biomarkers. This is the first study to compare between both procedures of DON exposure detection (diet study and human bio-monitoring approach) within the same population. Food and urine samples were collected from 199 healthy participants. The highest concentrations of DON and its derivatives were detected in wheat-based products. Both DON and its metabolite, DOM-1, were found in the urine samples. Total (free + conjugated) DON was detected in 99% of the samples, with a mean concentration at 109.21 ng mL^{-1}. The mean estimated dietary intake (EDI) level calculated from food consumption and contamination data was obtained as 2.54 ± 1.63 μg kg^{-1} bw d^{-1}, while the mean probable daily intake (PDI) based on urinary biomarkers was estimated to be 3.96 ± 4.20 μg kg^{-1} bw d^{-1}. A significant correlation was evidenced between EDI and PDI, both exceeding the provisional maximum tolerable daily intake. Elevated contaminant levels were observed in the adolescent group compared to children, adults, and elders, thereby indicating a potential health risk in them. The excretion rate of adolescents was approximately 2.5 times that of adult participants, possibly indicative of higher metabolic activity, which needs further in-depth investigation.

Keywords

deoxynivalenol; duplicate diet study; human bio-monitoring; urinary biomarkers; exposure assessment

1. Introduction

Deoxynivalenol (DON), a trichothecene mycotoxin produced by *Fusarium graminearum* and *F. culmorum,* is a predominant contaminant of wheat, maize, and barley throughout the world (Ali et al., 2016). Research has suggested that DON exposure in animals can prove to be toxic and cause serious problems such as emesis, anorexia, decreased body weight gain, cardiotoxicity, and immunotoxicity, as well as, impaired reproduction and development resulting from maternal toxicity (Payros et al., 2016). In view of the presence of widespread DON contamination in food and its toxic effects, many organisations and countries have set DON limit standards. In 2011, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) conducted a series of risk assessments and established a provisional maximum tolerable daily intake (PMTDI) of 1 μg kg^{-1} bw d^{-1} for DON and its acetylated derivatives, 3-acetyl-deoxynivalenol (3A-DON) and 15-acetyl-deoxynivalenol (15A-DON) (WHO, 2011). As per the Commission Regulation (EC) No. 1126/2007, the maximum DON levels in various foodstuffs were set as: unprocessed durum wheat and oats (1750 μg kg^{-1}), soft wheat (1250 μg kg^{-1}), bread, pastries, biscuits, cereal snacks and breakfast cereals (500 μg kg^{-1}), products such as dry pasta, cereals, cereal flour, bran, and germ meant for direct human consumption (750 μg kg^{-1}), and processed cereal-based baby foods and foods for young children (200 μg kg^{-1}). In China, the DON limit standards in grain and its products have been determined as 1000 μg kg^{-1} ((National Health Commission of PRC, 2017).

Deoxynivalenol contamination in crops is a common phenomenon reported across the world, including in countries like China, Japan, and the United States. Given its toxicity in animals and the potential health concerns in humans, it is necessary to conduct accurate DON exposure assessments. The two primary procedures for this include dietary exposure and biomarker-based exposure methods. As humans and animals are exposed to DON mainly by ingestion of contaminated food (Ali, Blaszkewicz, & Degen, 2016), calculation of the exposure levels based on food contamination levels and food consumption data has been well recognised as an effective and reliable way to assess human exposure to such mycotoxins via food. The exposure assessment of DON has been conducted in several countries and regions, such as the total diet studies (TDSs), in France (Sirot, Fremy, & Leblanc, 2013), Spain (Eduardo, María, Tania, Cristina, & Félix, 2013), Netherlands (Sprong et al., 2016), and China (Wu et al., 2015; Wu, Zhao, & Li, 2018). Biomarker-based exposure measurement in case of DON is essentially obtained using urinary biomarkers (considering the metabolic transformation of DON), and the concentrations of urinary DON can thus be employed to accurately assess their exposure risk in humans. Following ingestion, DON quickly disappears from the bloodstream and is excreted to the urine in the form of non-metabolised free DON, its phase I metabolite, de-epoxy-deoxynivalenol (DOM-1), and glucuronide conjugates (DON-GlcA) like DON-3-glucuronide (DON-3-GlcA) and DON-15-glucuronide (DON-15-GlcA). In humans, most of the ingested DON is metabolised as DON-GlcA (phase II metabolism), the process being catalysed by UDP-glucuronosyl-transferase.

In addition, the gut microbiota present in human intestine has been found to detoxify a small portion of DON to DOM-1, and conversion to glucuronide conjugates, which are then excreted in the urine (Gratz, Duncan, & Richardson, 2014). This approach has been adopted for internal exposure assessment of DON in some countries including Europe (UK, France, Croatia, Austria, Germany, Italy, Belgian, Spain, Swedish) (Cirlini et al., 2016; Föllmann, Ali et al., 2016; Gerding, Cramer, & Humpf, 2014; Hepworth et al., 2012; Heyndrickx et al., 2015; Huybrechts, Martins, Debongnie, Uhlig, & Callebaut, 2015; Papageorgiou et al., 2018a; Papageorgiou et al., 2018b; Rodriguez-Carrasco, Molto, Manes, & Berrada, 2014; Rodriguez-Carrasco, Manes, Berrada, & Font, 2015; Šarkanj et al., 2013; Solfrizzo, Gambacorta, & Visconti, 2014; Turner et al., 2008a; Turner et al., 2008b; Turner et al., 2010a; Turner et al., 2011; Warth et al., 2012; Wallin et al., 2015; Warth et al., 2016; Wells et al., 2016; Wells et al., 2017), Africa (South Africa, Egypt, Cameroon, Tanzania) (Abia et al., 2013; Gong, Shirima, Srey, Kimanya, & Routledge, 2015; Piekkola et al., 2012; Shephard et al., 2013; Srey, Kimanya, Routledge, Shirima, & Gong, 2014) , and Asia (Bangladesh and Shanghai, Yunnan, Henan, Anhui of China) (Ali, Blaszkewicz, Nahid, Rahman, & Degen, 2015; Ali, Blaszkewicz, & Degen, 2016; Ali, Manirujjaman, Rana, & Degen, 2020; Deng et al., 2018; Meky et al., 2003; Turner et al., 2011) .

The purpose of this study was to assess the dietary intake and biomarker-based exposure of DON among the residents of Anhui province in China, using the duplicate diet method and human bio-monitoring approach. The study groups

103 comprised of children, adolescents, adults, and elders of both genders. Such
104 diversified age groups were selected in order to understand the relation between the
105 dietary intake and internal exposure of DON, and whether gender and age played a
106 differential role in influencing it. Although several studies have investigated this
107 relationship, few have focused on adolescents and children. This study is the first
108 detailed analysis of the correlation and difference between dietary and internal DON
109 exposure in a considerably large population sample from a high-exposure area in
110 China.

111 ## 2. Materials and Methods

112 ### *2.1 Chemicals and reagents*

113 Mycotoxin standards for DON (100 μg mL^{-1}), DOM-1 (50 μg mL^{-1}), 3A-DON (100
114 μg mL^{-1}), 15A-DON (100 μg mL^{-1}), DON-3-G (50 μg mL^{-1}), and $^{13}C_{15}$-DON (10 μg
115 mL^{-1}) were purchased from Biopure (Tulln, Austria), while the enzyme
116 *β*-glucuronidase (Type IX from *E. coli*) was obtained from Sigma-Aldrich (MO,
117 USA). LC-MS gradient grade water, acetonitrile, methanol, formic acid, and
118 ammonium acetate were commercially obtained from Fisher Scientific (Leicestershire,
119 United Kingdom). All other chemicals and reagents used in this study were of
120 analytical grade or better. The Oasis PRiME HLB 96-well μElution plate (3 mg/30 μm)
121 was product of Waters (Milford, MA, USA). A mixed standard containing 10 μg mL^{-1}
122 of each of the analytes was prepared in ACN/H_2O (50/50, v/v) and stored at 4 ºC, and
123 working dilutions of the mixed standards were freshly prepared for each run in
124 methanol/H_2O (20/80, v/v). Similarly, the enzyme solution containing 2000 U mL^{-1} of

125 β-glucuronidase was also prepared freshly on each day of experimentation in a
126 phosphate buffer (0.075 mol L^{-1}, pH 6.8).

127 ***2.2 Study design and population samples***

128 This study was carried out in 2016 in select rural areas of the Anhui Province (i.e.,
129 Hao and Gao villages, Yingshang County, Fuyang City), located in east China. A
130 sample of 199 healthy volunteers (96 male and 103 female) from 74 families offering
131 homemade meals in Fuyang City were randomly chosen for the study and divided into
132 four age groups. Each family was given a family code and each family member was
133 further assigned a member code. All the participants were healthy volunteers. A short
134 medical check-up of the participants revealed no acute or chronic illnesses, except for
135 some infections of the upper respiratory tract. All participants consumed a mixed diet,
136 and none of them were on a special diet. The dietary DON intakes were measured by
137 the duplicate diet portion method, according to the WHO Guidelines (WHO, 1985).
138 Each individual's physiological information, food samples, and urine sample were
139 labelled with his/her unique number.

140 Samples of all cereal foods consumed by each participant during a single day
141 (entire day) within the study period were collected and transported to the laboratory
142 via the cold chain. In addition, we recorded the names and weights of all the food
143 items consumed. The collected food samples were then weighed, homogenised, and
144 subjected to analysis for detection of DON and DON metabolites. There were 244
145 duplicate diet food samples, which mainly included cereal products such as steamed
146 buns, noodles, rice porridges, boiled rice, baba (local pancakes made with glutinous

147 flour), baked pancakes, deep-fried dough sticks, cookies, dumplings, crispy rice,
148 sangza soup (crispy noodle soup), beer, steamed twisted rolls, cornmeal porridge, and
149 sweet potato porridge. Among these foods, 63 steamed buns, 64 noodles, 72 rice
150 porridges, 25 boiled rice, 7 baba, 3 dumplings, and 10 other foods were served.
151 Second-day morning urine samples were collected from each participant and
152 immediately transported to the laboratory, where it was stored frozen at -70 ℃ until
153 further analysis. The protocol of this study was approved by the ethics committee of
154 the China National Center for Food Safety Risk Assessment (No. 2016030063), and
155 all the experiments were performed according to the approved guidelines and
156 regulations. In the case of minors who participated in this study, informed consent
157 from their parents or guardians were duly sought.

158 ***2.3 Analytical procedure of DON assessment in food and urine samples***

159 The collected food and urine samples were thoroughly thawed and homogenised,
160 wherein the urine samples were centrifuged at 5000×g for 15 min to remove any
161 debris.

162 The presence of DON and its derivatives (deoxynivalenol-3-glucoside (DON-3-G),
163 3-and 15-acetyldeoxynivalenol (3A-DON and 15A-DON) and DOM-1 in the
164 collected food samples was analysed using the method specified by Wu (2015). The
165 internal standard ($^{13}C_{15}$-DON, 1 mg L^{-1}) was mixed into 2.0 g of the sample, followed
166 by extraction with 10 mL ACN/H_2O (86/14, v/v) with rigorous shaking for 1.5 h
167 before centrifugation at 9000×g for 15 min. The supernatant (5 mL) was further

168 cleaned via MultiSep®226 multifunctional column. The analytes were dried with N_2
169 and dissolved with 1 mL of ACN/H_2O (20/80, v/v) prior to LC-MS/MS analysis.

170 The analysis of urinary DON was performed based on our previous work- Deng et
171 al. (2018). The urine samples were spiked with the internal standard, $^{13}C_{15}$-DON, and
172 then 1 mL of the sample was digested with 2000 U of β-glucuronidase. The mixture
173 was incubated in a shaking water bath at 37 ℃ for 18 h for digestion. After being
174 cleaned via Oasis® PRiME HLB μElution Plate, the sample was analysed using
175 LC-MS/MS.

176 The identification and quantification of the contaminants was performed in an
177 ACQUITY UPLC™ I-Class system (Waters, MA, USA) connected to a Xevo® TQ-S
178 tandem quadrupole mass spectrometer (Waters, MA, USA), equipped with an
179 electrospray ionisation (ESI) source. Chromatographic separation of DON and its
180 metabolites was accomplished on a CORTECS™ UPLC® C18 Column (2.1×100 mm,
181 1.6 μm, Waters, MA, USA), detected under a multi reaction monitoring (MRM) mode,
182 and quantified by the isotope internal standard.

183 ***2.4 Dietary exposure assessment of DON***

184 *2.4.1 Estimated intake of DON from food*

185 The estimated daily intakes (EDI) of DON were calculated based on the food
186 consumption data of the surveyed population and concentrations of DON, 3A-DON,
187 and 15A-DON in the food samples. The formula is as follows (Wu, 2015):

188 $$EDI = \frac{\sum C \times m}{W}$$

where C = total concentration of DON, 3A-DON, and 15A-DON in food sample (μg kg^{-1}), m = food consumption (kg d^{-1}), W = the individual body weight of each participant (kg).

2.4.2 Probable intake of DON based on biomarkers present in daily urine excretion

The probable daily intake (PDI) of DON was calculated using urinary biomarkers based on the formula:

$$PDI = \frac{C \times V \times 100}{W \times E}$$

where C = total DON concentration (μg L^{-1}), V = daily urine excretion (L), W = body weight of each participant (kg), E = excretion rate (%). In the calculation, the mean daily urine excretion was assumed to be 0.5 L for children and 1.5 L for adults (Gong et al, 2015; Haga and Sakata, 2010). The excretion rate was considered to be 68%, with 52% as DON-glucuronides and 16% as free DON (Warth et al., 2013).

2.5 Statistical analysis

If the concentration of DON and its derivatives in the food and urine samples were below the limit of detection (LOD), then a value of half their respective LODs were considered for the statistical analysis (Haga et al., 2010; Piekkola et al., 2014). The independent sample t-test and ANOVA was employed to test for significant differences between the sub-groups at $p < 0.05$. Furthermore, the correlations of total DON with free DON and total DOM-1, and of EDI with PDI were analysed using the Spearman's rank correlation coefficient. All statistical analyses were conducted using SPSS, version 19 (SPSS, Chicago, IL, USA).

3. Results and Discussion

3.1 Demographic characteristics

The demographic characteristics of the participants are shown in Table 1. The 199 healthy volunteers (96 male, 103 female), aged between 4 to 80 years, from 74 households were divided into four groups. The children's group was aged ≤ 12 years; adolescents, 13-18 years; adults, 19-65; and elderly, > 65 years.

3.2 Duplicate diet analysis

3.2.1 Food consumption

The duplicate diet food samples collected from the study area were analysed for DON and its derivatives using the LC-MS method. Figure 1 presents the average consumption of each food category in the participants, calculated from their individual consumption data. Mean intake of steamed buns, noodles, rice porridges, boiled rice, baba, baked pancake, dumplings, deep-fried dough stick, crispy rice, sangza soup (crispy noodle soup), beer, steamed twisted rolls, cookies, cornmeal porridge, and sweet potato porridge was obtained as 205.19, 436.13, 544.87, 115.82, 16.11, 3.12, 32.40, 1.32, 1.70, 3.74, 2.51, 2.83, 0.25, 2.50, and 18.63 g d^{-1}, respectively. In China, the results of the fifth Chinese total diet study shows that the main cereal foods consumption of Chinese population are (924.62 g d^{-1}), beverages and water (891.58 g d^{-1}), vegetables (404.92 g d^{-1}), meats (95.77 g d^{-1}), legumes (87.55 g d^{-1}), potatoes (81.36 g d^{-1}) (Wu, 2015). Wheat and rice constitute the staple foods, although there may be regional variations in the consumption pattern. Similarly, in this study, steamed buns, noodles, rice porridges, boiled rice were observed to be the main types of staple food, of which rice porridge marked the highest consumption.

233 In the eastern region of China, there has been a decrease in the consumption of
234 maize since the 1980s. Similar changes in the consumption pattern could be observed
235 in the Anhui rural areas during our survey using the duplicate diet method.
236 Consequently, the intake of maize and other coarse cereals were less, as compared to
237 rice and wheat, which were the predominant cereals.

238 *3.2.2 Concentrations of DON in food samples*

239 Table 2 lists the mean and median concentrations, of DON and its derivatives
240 (DOM-1, DON-3-G, 3A-DON, and 15A-DON), their concentration ranges, and
241 detection rate in the duplicate diet food samples. As can be seen from the table, the
242 mean concentration of DON at 151.7 ± 223.0 μg kg^{-1} (ND ~ 1770 μg kg^{-1}) was the
243 highest, followed by DON-3-G levels at 18.32 ± 30.63 μg kg^{-1} (ND ~ 297.8 μg kg^{-1}).
244 Similarly, DON was the main contaminated toxin in terms of the detection rate,
245 followed by DON-3-G and DOM-1, while 3A-DON and 15A-DON displayed the
246 lowest rates.

247 Figure 2 shows the mean concentrations of DON and its derivatives in each food
248 category. As can be observed, the concentrations of these contaminants in wheat
249 (steamed buns, noodles, dumplings, and other wheat products) and glutinous rice
250 products (baba) were significantly higher than in rice products (rice porridge, boiled
251 rice, etc.). Furthermore, within the wheat products, steamed buns revealed higher
252 concentrations than dumplings and noodles.

253 Data from across the world has shown that DON and its derivatives (DON-3-G,
254 3A-DON and 15A-DON) mainly contaminate wheat, barley, oats, and maize, as

opposed to lesser contamination in rice and sorghum (Lu and Yang, 2015). In wheat and its associated products, the concentrations of DON, DON-3-G, 3A-DON, and 15A-DON are largely affected during the processing stage (Kostelanska et al., 2011; Pacin et al., 2010; Wu & Wang, 2016). Previously published data has suggested that DON concentration in steamed buns increased by nearly twice than its initial content in flour, while that of DON-3-G decreased significantly as it (and other derivatives) converted to DON (Zhang & Wang, 2014). Wu and Wang (2016) have reported that throughout the Chinese steamed bread making process, DON remains stable, while 3-ADON and 15-ADON get partially deacetylated and transform to DON during kneading (54.1–60.0% and 59.3–77.5%, respectively), fermentation (64.0–76.9% and 78.2–91.6%, respectively), and steaming (47.2–52.7% and 52.4–61.9%, respectively). On the contrary, during the process of cooking noodles, DON migrates to the cooking water given its high water solubility, thereby accounting for reduced concentrations of DON and DON-3-G in the cooked noodles (Moazami Farahany & Jinap, 2011).

In accordance with the findings of studies conducted both in China and elsewhere, all the dietary food samples examined in this study exhibited DON and DON-3-G as the most prevalent forms among the DON-related compounds. Of the 244 dietary samples collected in this study, the detection rate of DON was obtained as 70.5% (151.7 ± 223.0 μg kg^{-1}), and that of DON-3-G as 54.9% (18.32 ± 30.63 μg kg^{-1}). Another similar study in Anhui Province based upon 709 grain samples collected from 2010 to 2014 obtained 100% detection rate for DON (Jin et al., 2016). These results demonstrate the higher prevalence of DON in cereals in Anhui Province. The

277 contamination levels were observed to vary between different years, wherein the years
278 with more rainfall exhibited higher than usual levels. Hence, this highlights the
279 necessity for stronger surveillance and control of DON and its derivatives in cereals.

280 ***3.3 Estimated dietary intake of DON from food***

281 *3.3.1 Dietary intake of DON*

282 The Estimated dietary intake (EDI) of DON was calculated based on concentrations
283 of DON, 3A-DON, and 15A-DON in food and food consumption data and expressed
284 as μg kg^{-1} bw d^{-1}. As mentioned earlier, during the analysis, if the concentrations were
285 below the LOD, then a value of 1/2 LOD was used to produce the estimates. The EDI
286 of DON thus obtained ranged between 0.16 and 9.78μg kg^{-1} bw d^{-1}, with the mean
287 level 2.54±1.63μg kg^{-1} bw d^{-1}, and 171 of the 199 participants (85.9%) exceeded the
288 PMTDI value set by JECFA (1μg kg^{-1} bw d^{-1}).

289 Amongst the four age groups, children had the highest EDI, with the mean value at
290 2.68 ± 1.92μg kg^{-1} bw d^{-1}, respectively, but no significant difference was present with
291 other three groups ($P>0.05$) (Table 3). Similarly, no significant difference could be
292 found with regards to gender in all the age groups. As can be seen in Table 3, the mean
293 EDI calculated over the total number of participants was estimated to be 2.54±1.63μg
294 kg^{-1} bw d^{-1}, wherein both values exceeded the PMTDI. This indicated a high potential
295 risk for the subjects.

296 *3.3.2 Food contribution to dietary exposure*

297 The contributions of food categories to the dietary intake of DON were investigated
298 (Figure 3). Although the surveyed population in this study exhibited higher

consumption of rice and rice porridge, these food items accounted for only 4% and 1% of the dietary exposure sources of DON, respectively. In contrast, steamed buns and noodles accounted for 62% and 20%, respectively. The contribution of noodles to DON dietary exposure was lower than that of steamed buns, despite its consumption being higher, thereby showing consistency with the findings of previous studies.

3.4 Human bio-monitoring

3.4.1 Urinary DON biomarkers in the subjects

As was described in the methods, urinary DON as biomarkers were used in this study to detect the prevalence of free and total (free + conjugated) DON and its metabolites in a select population of the Anhui province. This study also evaluated the occurrence of free DON (fDON) and DOM-1 (fDOM-1) by eliminating the β-glucuronidase digestion step. Of the collected urine samples, 95.0% (n=189/199) showed positive detection for fDON and 14.6% (n=29/199) for fDOM-1. The mean fDON level was 22.47 ng mL^{-1} (range being below the LOD at 173.2 ng mL^{-1}), while fDOM-1 exhibited low levels in few of the samples with a mean of 0.18 ng mL^{-1}. Following enzymatic hydrolysis, urinary tDON was determined in 99.0% (n=197/199) of the samples, with a mean value of 109.2 ng mL^{-1} (<LOD range at 583.6 ng mL^{-1}). The detection rate obtained for tDOM-1 was 45.2% (n=90/199), with its mean concentration being 3.01 ng mL^{-1} (<LOD, range = 110.8 ng mL^{-1}) (Table 4). Thus, it was observed that the concentration of DON and DOM-1 increased substantially upon treatment with β-glucuronidase, indicating that glucuronide conjugates are the main metabolites of both DON and DOM-1. This is consistent with the findings of previous

321 studies (Chen et al., 2017; Warth et al., 2012; Turner et al., 2011).

322 Table 5 summarises the results of recent human bio-monitoring studies of urine
323 samples, wherein it is evident that the major metabolites of DON are DON-3-GlcA,
324 DON-15-GlcA, and DOM-1. Recently, the presence of DON-3-sulfate as a phase II
325 metabolite of DON has also been detected in human urine, and its concentration in the
326 excreted urine after 24 h was found to be approximately 4% of the initial DON intake
327 (Warth et al., 2016). Therefore, only β-glucuronidase was used in this study, where
328 the results can represent most of the DON urinary metabolites.

329 Human exposure to DON through contaminated food has been widely reported
330 from across the world (Asia, Europe, and Africa), as well as from different provinces
331 of China. In China, DON biomarker levels in urine have been reported in healthy
332 residents from Shanghai, Yunnan, and Henan. Nevertheless, the DON biomarker
333 levels pertaining to the Anhui province determined in our study are by far the highest.
334 These magnified levels indicate the regional and temporal variability of DON
335 exposure in the Chinese population. China has five main climatic zones, each with
336 diverse dietary habits and possibilities of food contamination, which ultimately
337 differentially influences the exposure to DON. Bangladesh, another Asian country,
338 also reported lower tDON values than those presented here. In addition, the overall
339 tDON values acquired in this study were notably higher than all those reported
340 previously from other regions, including Europe and Africa, excepting the results
341 obtained for pregnant women in Croatia (Šarkanj et al., 2013). We believe that the
342 urinary DON concentrations found in this study may well be the highest levels to be

343 recorded in Chinese populations, which could be partially attributed to the large
344 consumption of cereals in this area.

345 So far, the data on the occurrence of DOM-1 in humans are still limited. While
346 some studies detected urinary tDOM-1 following enzymatic hydrolysis by
347 *β*-glucuronidase at very low levels (Föllmann, 2016; Turner et al., 2010b; Turner et al.,
348 2011), others did not find any presence (Hepworth et al., 2012; Papageorgiou et al.,
349 2018a). Conversely, in our study, tDOM-1 was detected in 45.2% of the samples,
350 which is in agreement with the findings of Henan province in China (30.5%), France
351 (34%), Belgium (25%), and Germany (40%, 50%); but higher than that in Sweden
352 (8%), Spain (3.7%), UK (3%), and Egypt (2%) (Ali et al., 2015; Deng et al., 2018;
353 Huybrechts et al., 2015). Research has indicated that the production of DOM-1 may
354 be due to the degradation of DON (detoxification) by intestinal microorganisms
355 (Chen et al., 2017; Gratz et al., 2013). In a previously published work, Deng et al.
356 (2018) first identified the occurrence of fDOM-1 in human urine. In this study,
357 fDOM-1 was detected in 14.6% of the samples (mean 0.18 ng mL^{-1}). We also
358 discovered that the surveyed population had higher levels of tDOM-1 in their urine,
359 which might be attributed to the higher level of DON intake.

360 *3.4.2 Influence of gender and age on the biomarkers*

361 The tDON and tDOM-1 occurrence in urine were further analysed for gender and
362 age influences. There was no significant difference in the levels of either tDON or
363 tDOM-1 according to the gender. With respect to the age of the participants, the mean
364 concentration of tDON was about 1.5-fold higher in adolescents (175.5 ± 151.8 ng

365 mL^{-1}) and children (141.1 ± 107.3 ng mL^{-1}) than in adults (91.16 ± 96.39 ng mL^{-1})
366 and the elderly group (79.04 ± 6.49 ng mL^{-1}), with significant differences between the
367 four groups (Table 6). However, the tDOM-1 levels did not exhibit any significant
368 difference.

369 Recent studies have found significant gender-based variations in animal response to
370 DON exposure, but few studies have elucidated this in humans. In animals, including
371 mice and pigs, males were more sensitive to DON exposure than females. In humans,
372 no such significant gender-based differences have been found, as apparent from
373 studies conducted over various populations in Tanzania, the UK, and Italy (Gong et
374 al., 2015; Solfrizzo et al., 2014; Srey et al., 2014; Turner et al., 2010b), although
375 countries like Spain and Cameroon did display notable variations (Ediage et al., 2012;
376 Rodriguez-Carrasco et al., 2014). However, the small sample size of these studies
377 may not reflect the influence of gender differences in DON exposure in a statistical
378 significant or reliable manner. In contrast, this study used a larger sample size of 199
379 urine samples to evaluate the gender differences, wherein the results verify an absence
380 of significant variation with respect to both tDON and tDOM-1 exposures.

381 There is very little data on DON exposure in children and adolescents, although
382 they should receive more attention given their high food intake in terms of per
383 kilogram of body weight and possible differences in metabolism compared to adults.
384 As evident in Table 6, the mean concentrations of tDON were higher in adolescents
385 and children (though with no significant difference between them, p=0.526) as
386 compared to the means in adults and the elderly (p=0.001). This is similar to the

Spanish data provided by Rodriguez-Carrasco et al. (2014). However, in the UK, the mean tDON concentration was higher in children (41.6 ng mg^{-1} creatinine) than in adolescents (21.0 ng mg^{-1} creatinine) (Papageorgiou et al., 2018a). In Bangladesh, the average DON level was about 2-fold higher in infant (3.8 ± 2.9, max 6.8 ng mg^{-1}) than in children urines (1.6 ± 1.8, max 8.6 ng mg^{-1}) (Ali et al., 2020), probably owing to the smaller body size and higher relative dietary intake of DON contaminated foodstuff of infants compared with children. Regarding the analysis of DOM-1 in this study, no significant gender and age differences were revealed, but its occurrence in the excreted urine was similar amongst all members of the same family. This could possibly be related to the similar gut microbiota composition of the family members given their shared environment and diet, and thus identical intestinal degradation of DON to DOM-1.

The correlation comparison between different urinary biomarkers demonstrated significant relation between the levels of fDON and tDON (Figure 4a, r=0.890, P<0.01). Free DON accounts for only 20.1% of tDON, which indicates that about 80% of the tDON is present as conjugated forms (mainly D-3-GlcA and D-15-GlcA). This is in accordance with the findings of previous studies (Maul et al., 2012; Warth et al., 2012). These results confirm that the content of tDON post enzymatic pre-treatment tends to be much higher than in the absence of hydrolysis. Thus, compared to fDON, tDON proved to be a more important urinary biomarker in reflecting the dietary exposure to DON. On the contrary, a weak correlation existed between tDOM-1 and

408 tDON (Figure 4b, r=0.019, p<0.01) in the 90 positive samples, where urinary tDOM-1
409 concentration was only 8.59% of the tDON level.

410 ***3.5 Estimated dietary DON intake assessed from urinary biomarkers***

411 As can be seen in Table 7, the mean PDI of the participants in total were estimated as
412 3.96±4.20 μg kg^{-1} bw d^{-1}, both exceeding the PMTDI. About 80% of the participants
413 exceeded the PMTDI set by JECFA (1μg kg^{-1} bw d^{-1}) (Warth, et al., 2013).
414 Adolescents exhibited the highest PDI, with a mean of 7.49 ± 6.63μg kg^{-1} bw d^{-1},
415 respectively, and 89.3% exceeding the PMTDI. Their values were also notably higher
416 than the other three age groups (P<0.05). Children (mean = 4.21 ± 3.51μg kg^{-1} bw d^{-1}),
417 adults (3.22 ± 3.31μg kg^{-1} bw d^{-1}), and elderly (3.03 ± 3.05μg kg^{-1} bw d^{-1}) showed
418 relatively lower PDI, with no significant difference (P>0.05). Thus, the overall
419 obtained results indicate a high potential risk of exposure to DON via foodstuffs in
420 this area.

421 ***3.6 Relationship between dietary intake and DON exposure***

422 The EDI of DON obtained in this study 2.54±1.63μg kg^{-1} bw d^{-1} was slightly higher
423 than that reported from Lebanon (1.56μg kg^{-1} bw d^{-1}) and the United states (1.50μg
424 kg^{-1} bw d^{-1}); near similar to Norway (2.6μg kg^{-1} bw d^{-1}); and significantly higher than
425 that reported from most other countries, such as Denmark, the United Kingdom,
426 Belgium, Germany, France, Austria, Netherlands, Portugal, Canada, and Ireland,
427 where the values ranged from 0.17 to 0.37μg kg^{-1} bw d^{-1} (Raad et al., 2014; Sirot et al.,
428 2013). Likewise, the mean PDI acquired here 3.96±4.20μg kg^{-1} bw d^{-1} was slightly
429 lower than that reported from Belgium (5.9μg kg^{-1} bw d^{-1}) and close to Croatia (4.1μg
430 kg^{-1} bw d^{-1}), while significantly higher than countries such as Germany (0.3μg kg^{-1}

431 bw d^{-1}) and Haiti (0.27μg kg^{-1} bw d^{-1}) (Gerding et al., 2015; Gerding et al., 2014;
432 Šarkanj et al., 2013).

433 We also discovered that the level of DON through internal exposure was higher
434 than the dietary exposure levels (Table 8). There may be two possible reasons for this.
435 Firstly, we had collected morning urine samples for this study and the DON
436 concentrations tend to be approximately two times higher in the morning urine
437 compared to a 24-hour urine sample. This may lead to an overestimation of the
438 internal exposure (Warth et al., 2013). The second reason could be that all the
439 volunteers in this study live in the rural areas of the Anhui province, where they
440 continue to be exposed to DON related compounds through unintended environmental
441 and occupational conditions in addition to the dietary sources of exposure. The
442 majority of the study population had DON exposure exceeding the PMTDI. It is
443 possibly related to the local food consumption pattern. The consumption of cereals in
444 this area (1387 g/d) was higher than the national average (924.6 g/d from the 5^{th}
445 China Total Diet Study). Besides, the climate might be another reason. In 2016, the
446 average annual precipitation of Anhui Province was nearly 40% more than usual, the
447 highest since 1961. That might lead to an increase in mycotoxin production both in
448 field and during storage.

449 With respect to dietary exposure, there were no significant differences in terms of
450 gender or age, as opposed to internal exposure, where significant dissimilarity was
451 observed between the adolescent group and the others. It has been reported by
452 previous studies that a substantial amount of dietary DON can be rapidly excreted

within 24 h. Accordingly, an average excretion rate of 68% (including 52% as DON-glucuronides and 16% as free DON) in humans was used for the calculations in this study. The ratio of $EDI_{adolescents}/EDI_{adults}$ was thus achieved as 0.912, and 2.325 for $PDI_{adolescents}/PDI_{adults}$ was. This implies that the excretion rate of adolescents is approximately 2.5 times that of adult participants. Further investigations, which take into account age-specific excretion rates, may needed to be performed for accurate internal exposure assessment. Phase II metabolism of DON in humans lead to the formation of a substantial amount of DON-glucuronides, which is also excreted in urine. The fDON to tDON ratio may reflect the metabolic efficiency of each individual; the corresponding ratios obtained in this study for adolescent and adult groups being 25.95 and 22.91, respectively. This reflects a higher metabolic activity in adolescents than in adults, which could be responsible for the high excretion rate in adolescents. More attention would need to be focussed on this aspect in future studies.

Significant positive correlation was found between the EDI and PDI levels of DON, thereby reflecting the relation between dietary and internal exposures (Figure 5, $r=0.306$, $P<0.001$). Thus, it can be concluded that both food-based dietary exposure and biomarker-based internal exposure assessments can be used to evaluate human exposure to DON.

4. Conclusions

In conclusion, this study investigated the association between dietary and biomarker-based exposure to DON in humans in a high-risk area of China using the duplicate diet method and bio-monitoring approaches. The correlation between these

two approaches have seldom been studied previously, especially in the case of DON. Our study is the first DON exposure assessment from the perspective of both dietary exposure and human bio-monitoring conducted over a considerably large sample population. The results obtained from the duplicate diet study ascertain DON to be the predominant analyte in food samples. The cereal sources of wheat and glutinous rice are contaminated with relatively higher DON levels, with wheat contributing to over 80% of the DON intake. DON and DOM-1 were also frequently detected in the urine samples, though in lesser amounts. Total DON with a mean concentration of 109.2ng mL^{-1} was detected in 99% of the samples, which was higher than in most populations previously studied. There were no significant differences based on gender or age in dietary exposure, while internal exposure exhibited significant variations between the adolescent group and the others, but the same did not appear with respect to gender. The PDI of DON estimated from urinary biomarker levels was higher in adolescents than in children, adults, and elders. The excretion rate of adolescents was also found to be approximately 2.5 times that of adult participants. These conditions need to be further investigated, wherein age-specific excretion rates may assist accurate internal exposure assessments. Significant positive correlation was observed between the EDI and PDI, and 85.9% (data from the EDI) and 79.4% (data from the PDI) of the study population had DON exposures exceeding the PMTDI, indicating a potential health risk in the surveyed area. Effective measures, including rigorous control procedures and enhanced monitoring, need to be undertaken to reduce such risks.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (Grant No. 21806028 and 31871723), Beijing Natural Science Foundation (Grant No. 7184231), and CFSA "523" High Level Talents Development Project.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Abia, W.A., Warth, B., Sulyok, M., Krska, R., Tchana, A., Njobeh, P.B., Turner, P.C., Kouanfack, C., Eyongetah, M., Dutton, M., & Moundipa, P.F. (2013). Bio-monitoring of mycotoxin exposure in Cameroon using a urinary multi-biomarker approach. *Food Chem. Toxicol. 62,* 927-934. https://doi.org/10.1016/j.fct.2013.10.003.Ali, N., Blaszkewicz, M., Nahid, A.A., Rahman, M., & Degen, G.H. (2015). Deoxynivalenol Exposure Assessment for Pregnant Women in Bangladesh. *Toxins, 7,* 3845-3857. https://doi.org/10.3390/toxins7103845.

Ali, N., Blaszkewicz, M., & Degen, G.H. (2016). Assessment of deoxynivalenol exposure among Bangladeshi and German adults by a biomarker-based approach. *Toxicol. Lett. 258,* 20-28. https://doi.org/10.1016/j.toxlet.2016.06.006.

Ali, N., Manirujjaman, M., Rana, S., & Degen, G.H. (2020). Determination of aflatoxin M_1 and deoxynivalenol biomarkers in infants and children urines from

519 Bangladesh. *A rch. Toxicol. 94,* 3775-3786.
520 https://doi.org/10.1007/s00204-020-02857-5.
521 Chan-Hon-Tong, A., Charles, M.-A., Forhan, A., Heude, B., & Sirot. V. (2013).
522 Exposure to food contaminants during pregnancy. *Sci. the Total Environ. 458,*
523 27-35. https://doi.org/10.1016/j.scitotenv.2013.03.100.
524 Chen, L., Yu, M., Wu, Q., Peng, Z., Wang, D., Kuča, K., Yao, P., Yan, H., Nüssler,
525 A.K., Liu, L., & Yang, W. (2017). Gender and geographical variability in the
526 exposure pattern and metabolism of deoxynivalenol in humans: a review. *J.*
527 *Appl. Toxocol. 37,* 60-70. https://doi.org/10.1002/jat.3359.
528 Cirlini, M., Mazzeo, T., Roncoroni, L., Lombardo, V., Elli, L., Bardella, M.T.,
529 Agostoni, C., Doneda, L., Brighenti, F., Dall'Asta, C., & Pellegrini, N. (2016).
530 Are treated celiac patients at risk for mycotoxins? An Italian case-study. *Toxins*
531 *(Basel) 9,* 11. https://doi.org/10.3390/toxins9010011.
532 Deng, C.L., Li, C.L., Zhou, S., Wang, X.D., Xu, H.B., Wang, D., Gong, Y.Y.,
533 Routledge, M.N., Zhao, Y.F., & Wu, Y.N. (2018). Risk assessment of
534 deoxynivalenol in high-risk area of China by human biomonitoring using an
535 improved high throughput UPLC-MS/MS method. *Scientific Reports, 8,* 1-9.
536 https://doi.org/10.1038/s41598-018-22206-y.
537 Ediage, E.N., Di Mavungu, J.D., Song, S., Wu, A., Van Peteghem, C., & De Saeger, S.
538 (2012). A direct assessment of mycotoxin biomarkers in human urine samples
539 by liquid chromatography tandem mass spectrometry. *Analytica Chimica Acta,*
540 *741,* 58-69. https://doi.org/10.1016/j.aca.2012.06.038.

541 Ediage, E.N., Di Mavungu, J.D., Song, S., Sioen, I., & De Saeger, S. (2013).
542 Multimycotoxin analysis in urines to assess infant exposure: a case study in
543 Cameroon. *Environ. Int. 57-58,* 50-59.
544 https://doi.org/10.1016/j.envint.2013.04.002.
545 Eduardo, B., María, I., Tania, P., Cristina, R., & Félix, H. (2013). Development of
546 sensitive and rapid analytical methodology for food analysis of 18 mycotoxins
547 included in a total diet study. *Anal. Chim. Acta 783,* 39-48.
548 http://doi.org/10.1016/j.aca.2013.04.043.
549 Ezekiel, C.N., Warth, B., Ogara, I.M., Abia, W.A., Ezekiel, V.C., Atehnkeng, J.,
550 Sulyok, M., Turner, P.C., Tayo, G.O., Krska, R., & Bandyopadhyay, R. (2014).
551 Mycotoxin exposure in rural residents in northern Nigeria: a pilot study using
552 multi-urinary biomarkers. *Environ. Int. 66,* 138-145.
553 https://doi.org/10.1016/j.envint.2014.02.003.
554 Föllmann, W., Ali, N., Blaszkewicz, M., & Degen, G.H. (2016). Biomonitoring of
555 mycotoxins in urine: pilot study in mill workers. *J Toxicol. Environ. Health A,*
556 *79,* 1015-1025. https://doi.org/10.1080/15287394.2016.1219540.
557 Gerding, J., Cramer, B., & Humpf, H.U. (2014). Determination of mycotoxin
558 exposure in Germany using an LC-MS/MS multibiomarker approach. *Mol. Nutr.*
559 *Food Res. 58,* 2358-2368. https://doi.org/10.1002/mnfr.201400406.
560 Gerding, J., Ali, N., Schwartzbord, J., Cramer, B., Brown, D.L., Degen, G.H., Humpf,
561 H.U. (2015). A comparative study of the human urinary mycotoxin excretion
562 patterns in Bangladesh, Germany and Haiti using a rapid and sensitive

563 LC-MS/MS approach. *Mycotoxin Res. 31,* 127-136.
564 https://doi.org/10.1007/s12550-015-0223-9.
565 Gong, Y.Y., Shirima, C.P., Srey, C., Kimanya, M.E., & Routledge, M.N. (2015).
566 Deoxynivalenol and fumonisin exposure in children and adults in a family
567 study in rural Tanzania. *World Mycotoxin J, 8,* 553-560.
568 https://doi.org/10.3920/WMJ2015.1878.Gratz, S.W., Duncan, G., & Richardson,
569 A.J. (2013). The human fecal microbiota metabolizes deoxynivalenol and
570 deoxynivalenol-3-glucoside and may be responsible for urinary
571 deepoxy-deoxynivalenol. *Appl. Environ. Microbiol. 79,* 1821-1825.
572 https://doi.org/10.1128/AEM.02987-12.
573 Gratz, S. W., Richardson, A.J., Duncan, G., & Holtrop, G. (2014). Annual variation of
574 dietary deoxynivalenol exposure during years of different Fusarium prevalence:
575 A pilot biomonitoring study. *Food Addit. Contam. Part A, 31,* 1579-1585.
576 https://doi.org/10.1080/19440049.2014.937772.
577 Haga, M., & Sakata, T. (2010). Daily salt intake of healthy Japanese infants of 3-5
578 years based on sodium excretion in 24-hour urine. *J Nutr. Sci. Vitaminol. 56,*
579 305-310. https://doi.org/10.3177/jnsv.56.305.
580 Hepworth, S.J., Hardie, L.J., Fraser, L.K., Burley, V.J., Mijal, R.S., Wild, C.P., Azad,
581 R., Mckinney, P.A., & Turner, P.C. (2012). Deoxynivalenol exposure
582 assessment in a cohort of pregnant women from Bradford, UK. *Food Addit.*
583 *Contam. A, 29,* 269-276. https://doi.org/10.1080/19440049.2010.551301.
584 Heyndrickx, E., Sioen, I., Huybrechts, B., Callebaut, A., De Henauw, S., & De Saeger,

585 S. (2015). Human biomonitoring of multiple mycotoxins in the Belgian
586 population: Results of the BIOMYCO study. *Environ. Int. 84,* 82-89.
587 https://doi.org/10.1016/j.envint.2015.06.011.
588 Huybrechts, B., Martins, J.C., Debongnie, P., Uhlig, U., & Callebaut, A. (2015). Fast
589 and sensitive LC-MS/MS method measuring human mycotoxin exposure using
590 biomarkers in urine. Arch. *Toxicol. 89,* 1993-2005.
591 https://doi.org/10.1007/s00204-014-1358-8.
592 Jin, S.H., Liu, B.L., Cui, J., & Chen, Z.F. (2016). Survey on fungal toxin
593 contamination of grain and its products in Anhui province from 2010 to 2014.
594 *Anhui J Prev Med. 22,* 340-342 (in Chinese).
595 Kostelanska, M., Dzuman, Z., Malachova, A., Capouchova, I., Prokinova, E.,
596 Skerikova, A., & Hajslova, J. (2011). Effects of milling and baking technologies
597 on levels of deoxynivalenol and its masked form deoxynivalenol-3-glucoside. *J*
598 *Agr. Food Chem. 59,* 9303-9312. https://doi.org/10.1021/jf202428f.
599 Lu, J.J., & Yang, D.J. (2015). Pollution investigation of deoxynivalenol in wheat flour
600 of China in 2013. *Journal of Hygiene Research, 44,* 658-660 (in Chinese).
601 Maul, R., Warth, B., Kant, J. S., Schebb, N. H., Krska, R., Koch, M., & Sulyok, M.
602 (2012). Investigation of the hepatic glucuronidation pattern of the fusarium
603 mycotoxin deoxynivalenol in various species. *Chem. Res. Toxicol. 25,*
604 2715-2717. https://doi.org/10.1021/tx300348x.
605 Meky, F.A., Turner, P.C., Ashcroft, A.E., Miller, J.D., Qiao, Y.L., Roth, M.J., & Wild,
606 C.P. (2003). Development of a urinary biomarker of human exposure to

607 deoxynivalenol. *Food Chem Toxicol, 41,* 265-273.
608 https://doi.org/10.1016/s0278-6915(02)00228-4.
609 Moazami Farahany, E., & Jinap, S. (2011). Influence of noodle processing (industrial
610 protocol) on deoxynivalenol. *Food Control, 22,* 1765-1769.
611 https://doi.org/10.1016/j.foodcont.2011.04.011.
612 National Health Commission of PRC. (2017). National food safety
613 standards—maximum residue limits of mycotoxins in food. GB2761-2017.
614 Standards Press of China. (In Chinese), Beijing.
615 Pacin, A., Bovier, E.C., Cano, G., Taglieri, D., & Pezzani, C.H. (2010). Effect of the
616 bread making process on wheat flour contaminated by deoxynivalenol and
617 exposure estimate. *Food Control, 21,* 492-495.
618 https://doi.org/10.1016/j.foodcont.2009.07.012.
619 Papageorgiou, M., Wells, L., Williams, C., White, K., De Santis, B., Liu, Y.,
620 Debegnach, F., Miano, B., Moretti, G., Greetham, S., Brera, C., Atkin, S. L.,
621 Hardie, L. J., & Sathyapalan, T. (2018a). Assessment of urinary deoxynivalenol
622 biomarkers in UK children and adolescents. *Toxins, 10,* 50-63.
623 https://doi.org/10.3390/toxins10020050.
624 Papageorgiou, M., Wells, L., Williams, C., White, K.L.M., De Santis, B., Liu, Y.,
625 Debegnach, F., Miano, B., Moretti, G., Greetham, S., Brera, C., Atkin, S.L.,
626 Hardie, L.J., & Sathyapalan, T. (2018b). Occurrence of deoxynivalenol in an
627 elderly cohort in the UK: A biomonitoring approach. *Food Addit. Contam. A, 35,*
628 2032-2044. https://doi.org/10.1080/19440049.2018.1508890.

629 Payros, D., Alassane-Kpembi, I., Pierron, A., Loiseau, N., Pinton, P., & Oswald, I.P.
630 (2016). Toxicology of deoxynivalenol and its acetylated and modified forms.
631 *Arch. Toxico. 90,* 2931-2957. https://doi.org/10.1007/s00204-016-1826-4.
632 Piekkola, S., Turner, P.C., Abdel-Hamid, M., Ezzat, S., El-Daly, M., El-Kafrawy, S.,
633 Savchenko, E., Poussa, T., Woo, J.C.S., Mykkänen, H., & El-Nezami, H. (2012).
634 Characterisation of aflatoxin and deoxynivalenol exposure among pregnant
635 Egyptian women. *Food Addit. Contam. A, 29,* 962-971.
636 https://doi.org/10.1080/19440049.2012.658442.
637 Raad, F., Nasreddine, L., Hilan, C., Bartosik, M., & Parent-Massin, D. (2014). Dietary
638 exposure to aflatoxins, ochratoxin A and deoxynivalenol from a total diet study
639 in an adult urban Lebanese population. *Food Chem. Toxicol. 73,* 35-43.
640 https://doi.org/10.1016/j.fct.2014.07.034.
641 Rodriguez-Carrasco, Y., Molto, J.C., Manes, J., & Berrada H. (2014). Exposure
642 assessment approach through mycotoxin/creatinine ratio evaluation in urine by
643 GC-MS/MS. *Food Chem. Toxicol. 72,* 69-75.
644 https://doi.org/10.1016/j.fct.2014.07.014.
645 Rodriguez-Carrasco, Y., Manes, J., Berrada, H., & Font, G. (2015). Preliminary
646 estimation of deoxynivalenol excretion through a 24h pilot study. *Toxins (Basel)*
647 *7,* 705-718. https://doi.org/10.3390/toxins7030705.
648 Šarkanj, B., Warth, B., Uhlig, S., Abia, W.A., Sulyok, M., Klapec, T., Krska, R., &
649 Banjari, I. (2013). Urinary analysis reveals high deoxynivalenol exposure in
650 pregnant women from Croatia. *Food Chem. Toxicol. 62,* 231-237.

https://doi.org/10.1016/j.fct.2013.08.043.

Shephard, G.S., Burger, H.M., Gambacorta, L., Gong, Y.Y., Krska, R., Rheeder, J.P., Solfrizzo, M., Srey, C., Sulyok, M., Visconti, A., Warth, B., & Westhuizen, L. (2013). Multiple mycotoxin exposure determined by urinary biomarkers in rural subsistence farmers in the former Transkei, South Africa. *Food Chem. Toxicol. 62,* 217-225. https://doi.org/10.1016/j.fct.2013.08.040.

Sirot, V., Fremy, J.M., & Leblanc, J.C. (2013). Dietary exposure to mycotoxins and health risk assessment in the second French total diet study. *Food Chem. Toxicol. 52,* 1-11. https://doi.org/10.1016/j.fct.2012.10.036.

Solfrizzo, M., Gambacorta, L., & Visconti, A. (2014). Assessment of Multimycotoxin exposure in Southern Italy by urinary multi-biomarker determination. *Toxins, 6,* 523-538. https://doi.org/10.3390/toxins6020523.

Sprong, R.C., De, W.L., Te, B.J.D., Alewijn, M., Lopez, P., & Mengelers, M.J.B. (2016). A mycotoxin-dedicated total diet study in the netherlands in 2013: Part iii—Exposure and risk assessment. *World Mycotoxin J. 9,* 109-128. https://doi.org/10.3920/WMJ2015.1905.

Srey, C., Kimanya, M.E., Routledge, M.N., Shirima, C.P., & Gong, Y.Y. (2014). Deoxynivalenol exposure assessment in young children in Tanzania. *Mol. Nutr. Food Res. 58,* 1574-1580. https://doi.org/10.1002/mnfr.201400012.

Turner, P.C., Burley, V.J., Rothwell, J.A., White, K.L., Cade, J.E., & Wild, C.P. (2008a). Dietary wheat reduction decreases the level of urinary deoxynivalenol in UK adults. *J Expo. Sci. Env. Epid. 18,* 392-399.

673 https://doi.org/10.1038/sj.jes.7500611.
674 Turner, P.C., Rothwell, J.A., White, K.L.M., Gong, Y.Y., Cade, J.E., & Wild, C.P.
675 (2008b). Urinary deoxynivalenol is correlated with cereal intake in individuals
676 from the United Kingdom. Environ. *Health Persp. 116,* 21-25.
677 https://doi.org/10.1289/ehp.10663.
678 Turner, P.C., Hopton, R. P., Lecluse, Y., White, K.L.M., Fisher, J., & Lebailly, P.
679 (2010a). Determinants of urinary deoxynivalenol and deepoxy deoxynivalenol
680 in male farmers from Normandy, France. *J. Agr. Food Chem. 58,* 5206-5212.
681 https://doi.org/10.1021/jf100892v.
682 Turner, P.C., White, K.L., Burley, V.J., Hopton, R.P., Rajendram, A., Fisher, J., Cade, J.
683 E., & Wild, C.P. (2010b). A comparison of deoxynivalenol intake and urinary
684 deoxynivalenol in UK adults. *Biomarkers, 15,* 553-562.
685 https://doi.org/10.3109/1354750X.2010.495787.
686 Turner, P.C., Ji, B.T., Shu, X.O., Zheng, W., Chow, W.H., Gao, Y.T., & Hardie, L.J.
687 (2011). A biomarker survey of urinary deoxynivalenol in China: the Shanghai
688 Women's Health Study. *Food Addit Contam A, 28,* 1220-1223.
689 https://doi.org/10.1080/19440049.2011.584070.
690 Turner, P. C. et al. Assessment of deoxynivalenol metabolite profles in UK adults.
691 Food Chem. Toxicol. 49, 132–135 (2011).
692 Wallin, S., Gambacorta, L., Kotova, N., Lemming, E.W., Nälsen, C., Solfrizzo, M., &
693 Olsen, M. (2015). Biomonitoring of concurrent mycotoxin exposure among
694 adults in Sweden through urinary multi-biomarker analysis. *Food Chem.Toxicol.*

695 *83,* 133-139. https://doi.org/10.1016/j.fct.2015.05.023.
696 Warth, B., Sulyok, M., Fruhmann, P., Berthiller, F., Schuhmacher, R., Hametner, C.,
697 Adam, G., Frohlich, J., & Krska, R. (2012). Assessment of human
698 deoxynivalenol exposure using an LC–MS/MS based biomarker method.
699 *Toxicol. Lett. 211,* 85-90. https://doi.org/10.1016/j.toxlet.2012.02.023.
700 Warth, B., Favero, G.D., Wiesenberger, G., Puntscher, H., Woelflingseder, L.,
701 Fruhmann, P., Sarkanj, B., Krska, R., Schuhmacher, R., Adam, G., & Marko, D.
702 (2016). Identification of a novel human deoxynivalenol metabolite enhancing
703 proliferation of intestinal and urinary bladder cells. *Sci Rep 6,* 33854.
704 https://doi.org/10.1038/srep33854.
705 Wells, L., Hardie, L., Williams, C., White, K., Liu, Y., De Santis, B., Debegnach, F.,
706 Moretti, G., Greetham, S., Brera, C., Rigby, A., Atkin, S., & Sathyapalan, T.
707 (2016). Determination of deoxynivalenol in the urine of pregnant women in the
708 UK. *Toxins (Basel) 8,* 306. https://doi.org/10.3390/toxins8110306.Wells, L.,
709 Hardie, L., Williams, C., White, K., Liu, Y., De Santis, B., Debegnach, F.,
710 Moretti, G., Greetham, S., Brera, C., Papageorgiou, M., Thatcher, N.J., Rigby,
711 A., Atkin, S., & Sathyapalan, T. (2017). Deoxynivalenol biomarkers in the urine
712 of UK vegetarians. *Toxins (Basel) 9,* 196.
713 https://doi.org/10.3390/toxins9070196.
714 World Health Organization (WHO). (1985). Guidelines for the study of dietary
715 intakes of chemical contaminants. GEMS: Global Environmental Monitoring
716 System, Kenya.

World Health Organization (WHO). (2011). Evaluation of certain contaminants in food. 72nd Report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), Geneva, Switzerland.

Wu, L., & Wang, B. (2016). Transformation of deoxynivalenol and its acetylated derivatives in Chinese steamed bread making, as affected by pH, yeast, and steaming time. *Food Chem. 202,* 149-155. https://doi.org/10.1016/j.foodchem.2016.01.124.

Wu, Y.N. (2015). *The Fourth China's total diet study.* Chemical Industry Press: Beijing, China.

Wu, Y.N., Zhao, Y.F., & Li, J.G. (2018). *The Fifth China Total Diet Study.* Science Press: Beijing, China.

Zhang, H., & Wang, B. (2014). Fate of deoxynivalenol and deoxynivalenol-3-glucoside during wheat milling and Chinese steamed bread processing. *Food Control, 44,* 86-91. https://doi.org/10.1016/j.foodcont.2014.03.037.

732 **Figure Captions**

733 **Figure 1** Mean weights of each food consumed per day (g d^{-1})

734 **Figure 2** Mean concentrations of DONs (μg kg^{-1})

735 **Figure 3** Distribution of various food sources of dietary DON and its derivatives in

736 the examined Anhui food samples.

737 **Figure 4** Scatterplot of urinary fDON (a) and tDOM-1 (b) against urinary tDON

738 **Figure 5** Scatterplot of DON dietary exposure and DON internal exposure

739 **Table 1** Demographic characteristics of the subjects (mean ± SD (range))

Variables	Children	Adolescents	Adults	Elderly
	Age≤12	12<Age≤18	18<Age≤65	Age>65
Number of subjects	37	28	83	51
Male	16	15	40	25
Female	21	13	43	26
Age (years)	6.8±2.3	14.5±1.3	42.3±14.0	70.4±3.7
Body Weight (kg)	25.0±7.2 (13-50)	53.1±10.2 (36-75)	62.2±9.0 (40-85)	58.7±10.2 (44-104)
BMI (kg/m^2)	17.7±4.3	20.2±3.3	22.6±2.9	22.4±3.0

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742 **Table 2** Levels of DON and derivatives in food samples (μg kg^{-1})

	Positive	Mean ± SD (μg kg^{-1})	Median (μg kg^{-1})	Range (μg kg^{-1})
DON	172 (70.5%)	151.7 ± 223.0	30.92	ND~1770
DOM-1	133 (54.5%)	1.10 ± 1.65	0.15	ND~12.97
DON-3-G	134 (54.9%)	18.32 ± 30.63	2.44	ND~297.8
3A-DON	15 (6.1%)	0.50 ± 0.47	0.35	ND~3.73
15A-DON	1 (0.4%)	0.84 ± 0.44	0.70	ND~5.05

743 ND, level below LOD; positive samples refer to the levels higher than LOD.
744

745 **Table 3** Estimated Dietary Intake of DON across the four examined age groups

Age	Gender	Mean (±SD)	Median	Range	Exceeding PMTDI
		μg kg^{-1} bw	μg kg^{-1} bw d^{-1}	μg kg^{-1} bw d^{-1}	n (%)
Age≤12	M(16)	2.23 (±1.99)	1.78	0.25-6.50	11(68.8)
	F(21)	3.02 (±1.79)	2.98	0.32-7.56	18(85.7)
	37	2.68 (±1.92)	2.19	0.25-7.56	29(78.4)
12<Age≤18	M(15)	2.26 (±1.18)	2.06	0.61-5.12	14(93.3)
	F(13)	2.47 (±1.21)	2.11	0.75-4.72	11(84.6)
	28	2.36 (±1.20)	2.08	0.61-5.12	25(89.3)
18<Age≤65	M(40)	2.71 (±1.75)	2.14	0.59-7.36	36(90.0)
	F(43)	2.48 (±1.88)	2.04	0.16-9.78	36(83.7)
	83	2.59 (±1.82)	2.11	0.16-9.78	72(86.7)
Age>65	M(25)	2.64 (±1.21)	2.35	0.92-6.09	24(96.0)
	F(26)	2.31 (±1.15)	2.10	0.72-4.81	21(80.8)
	51	2.31 (±1.19)	2.23	0.72-6.09	45(88.2)
Total	199	2.54 (±1.63)	2.19	0.16-9.78	171(85.9)

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747 **Table 4** Summary of free and total DON and it's metabolites in 199 urine samples

	Free				Total			
compound	positive	mean	median	range	positive	mean	median	range
	n(%)	μg L^{-1}	μg L^{-1}	μg L^{-1}	n(%)	μg L^{-1}	μg L^{-1}	μg L^{-1}
DON	189(95.0)	22.47	12.00	ND- 173.3	197(99.0)	109.2	77.47	ND-583.6
DOM-1	29(14.6)	0.18	ND	ND-11.06	90(45.2)	3.01	ND	ND-110.8

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Table 5 Occurrence of DON and its metabolites in human urine

Countries	Sample(n)	Gender	Age	Positive n (Analyte)	Mean/median, ng mL^{-1}	range, ng mL^{-1}	References
Europe							
UK	25	16(M) 9(F)	21-59	25 (DON)	7.2(Geometric mean) creatintine	4.9-10.5 creatintine	Turner et al., 2008a
UK	300	-	-	296(DON)	9.42 μg/day	ND-65.97 μg/day	Turner et al., 2008b
France	76	-	23-74	75(DON)	6.8	0.8-28.8	Turner et al., 2010a
				26(DOM-1)	0.2	0.2-2.8	
UK	35	17(M) 18(F)	20-59	23 (DON+DON- GlcA)	17.8/13.8	5.0-78.2	Turner et al., 2011
				23 (DON)	2.4	0.5-9.3	
				1 (DOM-1)	0.3	<LOD -0.8	
UK	85	pregnant	16-44	85(DON)	10.3 creatintine	0.5-116.7	Hepworth et al., 2012
				0(DOM-1)	<LOD	<LOD	
UK	42	pregnant	20-38	On 1 day: 37 (DON+ DON-GlcA)	29.7	<LOD-436.0	Wells et al., 2016
				On 2 day: 35 (DON+ DON-GlcA)	28.7	<LOD-167.0	
				0 (DOM-1)	<LOD	<LOD	
				0 (DOM-GlcA)	<LOD	<LOD	
UK	63	11(vegetarian M)	-	On 1 day: (tDON)	13.6	<LOD-39.1	Wells et al., 2017
			-	On 2 day: (tDON)	14.5	<LOD-55.4	
		21(vegetarian F)		On 1 day: 17 (tDON)	31.1	<LOD-135.0	
				On 2 day: 19 (tDON)	22.9	<LOD-60.5	
		16 (Adult M)	18-64	On 1 day: (tDON)	13.1	2.20-29.4	
				On 2 day: (tDON)	18.1	5.10-58.8	
		15 (Adult F)	18-64	On 1 day: (tDON)	12.4	3.30-40.6	

				On 2 day: (tDON)	14.2	0.90-36.0	
UK	40	20(M) 20(F)	3-9	On 1 day: (tDON)	M: 22.5 F: 38.2	M:1.2-86.5 F:3.0-138.0	Papageorgiou et al.,
				On 2 day: (tDON)	M: 20.6 F: 35.4	M:4.1-52.0 F:1.4-140.9	2018a
	39	19(M) 20(F)	10-17	On 1 day: (tDON)	M: 20.6 F: 26.0	M:1.6-52.5 F:3.1-104.3	
				On 2 day: (tDON)	M: 27.0 F: 28.8	M:2.9-66.3 F: <LOD -67.2	
UK	20	10(M) 10(F)	≥65	On 1 day: 9, 9 (tDON)	M: 26.7 F: 8.0	M: <LOD -186.0 F: <LOD -28.8	Papageorgiou et al.,
				7, 9 (fDON)	M: 5.0 F: 0.8	M: <LOD -42.0 F:0.1-1.8	2018b
				9, 9 (DON-GlcA)	M: 21.7 F: 7.3	M: <LOD -144.0 F: <LOD -27.0	
				0, 0 (DOM-1)	M: <LOD F: <LOD	M: <LOD F: <LOD	
				On 2 day: 9, 9 (tDON)	M: 20.1 F: 8.8	M: <LOD -65.1 F: <LOD -17.5	
				6, 7 (fDON)	M: 2.2 F: 1.0	M: <LOD -11.8 F: <LOD -3.3	
				9, 9 (DON-GlcA)	M: 17.8 F: 7.8	M: <LOD -53.3 F: <LOD -14.2	
				0, 0 (DOM-1)	M: <LOD F: <LOD	M: <LOD F: <LOD	
Croatia	40	pregnant	26-33	39 (DON-15GlcA)	120.4/55.2	<LOD-1237.7	Šarkanj et al., 2013
				33 (DON-3GlcA)	28.8/10.0	<LOD-298.1	
				31 (fDON)	18.3/6.7	<LOD-275.0	
Croatia	40	pregnant	26-33	28 (DON-3-sulfate)	4.5	<LOD-58.0	Warth et al., 2016
Austria	27	-	20-63	tDON: 6(fDON)+26(DON-GlcA's)	20.4/2.4	<LOQ-63	Warth et al., 2012
Germany	101	44(M)	20-30	30 (fDON)	5.3/3.38	5.97-31.31	Gerding et al., 2014
				84 (DON-GlcA)	15.51/9.41	2.95-139.37	
Italy	52	26(M) 26(F)	3-85	50 (fDON)	11.89 /10.32	<LOD -67.36	Solfrizzo et al., 2014
Italy	55	celiac patient	-	4 (fDON)	0.22/0.00	<LOQ-8.94	Cirlini et al., 2016
				5 (DON-GlcA)	0.22/0.00	<LOQ-5.59	
	50	healthy subject	-	4 (fDON)	0.17/0.00	<LOQ-2.41	
				5 (DON-GlcA)	0.17/0.00	<LOQ-5.84	
Belgian	32	-	-	32 (DON-15GlcA)	82.62	3.00 -420	Huybrechts et al.,

				29 ((DON-3GlcA)	10.65	<LOQ-550	2015
				8 (DOM-GlcA)	4.60	0.80-16.4	
				23 (DON)	0.436	<LOD -3.00	
Belgian	239	-	19-65	238 (DON-15GlcA)	53.8/31.2	<LOQ-460.8	Heyndrickx et al.,
				184 ((DON-3GlcA)	7.5/4.4	<LOQ-126.2	2015
				53 (DOM-GlcA)	16.9/5.8	<LOD -172.0	
				89 (DON)	3.9/1.7	<LOD -129.8	
	155	-	3-12	155 (DON-15GlcA)	58.4/42.6	4.6-301.7	
				141 ((DON-3GlcA)	10.6/7.8	<LOQ-53.0	
				26 (DOM-GlcA)	91.7/24.0	<LOD -526.1	
				109 (DON)	5.2/3.9	<LOD -27.4	
Spain	54	16	8-14	9（DON）	DON:27.8 creatintine	<LOD -84.5	Rodriguez-Carrasco,
				1 (DOM-1)	DOM-1:1.3	<LOD -1.3	2014
		16	18-28	12（DON）0 (DOM-1)	creatintine	<LOD -69.1	
		22	＞28	16（DON）0 (DOM-1)	DON:32.9 creatintine	<LOD -56.9	
					DON:14.8 creatintine		
Spain	1	Male	26	1(fDON)	18.8	18.8	Rodriguez-Carrasco,
							2015
Swedish	252	-	-	158 (DON)	3.37	-	Wallin et al., 2015
				20 (DOM-1)	0.18	-	
Germany	30	13(Male control)	-	13 (DON)	6.85/6.794	1.013-14.634	Föllmann et al., 2016
				5 (DOM-1)	0.085/0.05	LOD -0.184	
		12(Male worker)		12 (DON)	6.50/5.395	3.275-13.82	
				7 (DOM-1)	0.105/0.114	LOD -0.216	
		5(Male worker)		5 (DON)	8.084//9.326	0.85-10.395	
				3 (DOM-1)	0.11/0.11	LOD -0.228	

Africa							
South Africa	53	Male	19-97	7 (DON)	1.52	<LOD -21.3	Shephard et al., 2013
Egypt	93	pregnant	18-40	63 (DON)	2.8(Geometric mean)	2.1-3.6	Piekkola et al., 2012
Cameroon	145	Male	18-58	8 (fDON)	<LOD	<LOD	Abia et al., 2013
				62 (DON-15GlcA)	5.49	<LOD -96.2	
				16 (DON-3GlcA)	3.93	<LOD -22.5	
				62 (tDON)	5.93	<LOD -74.69	
Tanzania	166	-	6-14 months	32 (tDON):Vist1	1.1	0.8-1.4	Srey et al., 2014
				40 (tDON):Vist2	2.3	1.7-3.2	
				38 (tDON):Vist3	5.7	4.1-7.9	
Tanzania	141	Children: 50		(DON)	15.4	10.2-23.3	Gong et al., 2015
		Mothers: 50 Fathers: 50		(DON)	45.0	31.8-63.6	
				(DON)	42.0	30.9-56.9	
Asia							
Bangladesh	54	pregnant	18-36	28 (fDON)	0.86/0.19	<LOD -7.16	Ali et al., 2015
				0 (DOM-1)	<LOD	<LOD	
Bangladesh	62	31(M) 31(F)	22-60	Summer: 17((fDON)	0.17/<LOD	<LOD -1.78	Ali et al., 2016
				0 (DOM-1)	<LOD	<LOD	
Bangladesh	154	Infants:49	1-12 months	3 (fDON)	3.8/3.67	<LOD -6.8	Ali et al., 2020
				0 (DOM-1)	<LOD	<LOD	
		Children:105	1-6 years	37 (fDON)	1.6/1.0	<LOD -8.6	
				0 (DOM-1)	<LOD	<LOD	
China	60	Female	40-70	0 (DOM-1)	5.9 creatintine	<LOD -30.5	Turner et al., 2011
(Shanghai)							
China	15	-	-	(DON)	Linxian: 37	14-94	Meky et al., 2003
(Yunnan)					Gejiu: 12	4-18	
China	150	56 (M) 95 (F)	2-78	140 (fDON)	8.25/5.48	<LOD -47.0	Deng et al., 2018
(Henan)				3 (fDOM-1)	0.052/0.05	<LOD -0.23	
				151 (tDON)	47.6/32.5	1.36 -247.0	

			46 (tDOM -1)	0.28/0.05	<LOD -6.43	
China	199	96 (M) 103 (F)	189 (fDON)	22.47	<LOD -173.2	This study
(Anhui)			29 (fDOM-1)	0.18	<LOD -11.06	
			197 (tDON)	109.2	<LOD -583.6	
			90 (tDOM-1)	3.01	<LOD -110.8	

750 **Table 6** Urinary tDON and tDOM-1 by gender and age groups

	fDON				tDON				tDOM-1			
	positive n (%)	mean μg L^{-1}	median μg L^{-1}	range μg L^{-1}	positive n(%)	mean μg L^{-1}	median μg L^{-1}	range μg L^{-1}	positive n(%)	mean μg L^{-1}	median μg L^{-1}	range μg L^{-1}
Gender												
Male n=96	92 (95.8%)	24.40 (±31.14)	13.18	ND-173.3	96 (100.0%)	114.6 (±117.2)	82.81	6.32-583.6	42 (43.8%)	3.13 (±9.31)	ND	ND-67.40
Female n=103	97 (94.2%)	20.66 (±23.90)	11.86	ND-138.1	101 (98.1%)	104.2 (±101.7)	72.16	ND-544.0	48 (46.6%)	2.89 (±12.11)	ND	ND-110.8
					P＞0.05				P＞0.05			
Age												
Age≤12, n=28	36 (97.3%)	26.38 (±20.85)	18.24	ND-82.01	37 (100.0%)	141.1 (±107.3)	91.74	15.15-500.7	16 (43.2%)	5.16 (±18.84)	ND	ND-110.8
12<Age≤18, n=28	27 (96.4%)	42.36 (±40.82)	29.72	ND-173.3	28 (100.0%)	175.5 (±151.8)	122.3	19.33-583.6	18 (64.3%)	4.03 (±10.13)	1.02	ND-49.27
18<Age≤65, n=83	78 (94.0%)	18.17 (±23.38)	10.15	ND-138.1	82 (98.8%)	91.16 (±96.39)	61.14	ND-499.8	28 (33.7%)	1.31 (±4.40)	ND	ND-36.06
Age>65, n=51	48 (94.1%)	15.69 (±78.24)	61.83	ND-154.9	50 (98.0%)	79.04 (±6.49)	2.48	ND-482.1	28 (54.9%)	3.67 (±10.23)	0.10	ND-67.40
					group 1,2 P＞0.05 group 3,4 P＞0.05 group 1,3 P=0.001 group 1,4 P=0.002 group 2,3 P=0.001 group 2,4 P=0.001				P＞0.05			

751 ND: level below LOD; positive samples refer to the levels higher than LOD.

752 group1: Age≤12; group2: 12<Age≤18; group3: 18<Age≤65; group4: Age>65

753 **Table 7** PDI of DON by 4 age groups

Age	Gender	Mean (±SD)	Median	Range	Exceeding PMTDI
		μg kg^{-1} bw	μg kg^{-1} bw d^{-1}	μg kg^{-1} bw d^{-1}	n(%)
Age≤12	M (16)	3.55 (±3.56)	1.70	0.86-14.73	13(81.3)
	F (21)	4.71 (±3.38)	4.15	0.69-14.80	19(90.5)
	37	4.21 (±3.51)	3.54	0.69-14.80	32(86.5)
12<Age≤18	M (15)	7.21 (±6.17)	4.58	0.57-23.41	13(86.7)
	F (13)	7.80 (±7.10)	4.97	0.62-26.66	12(92.3)
	28	7.49 (±6.63)	4.89	0.57-26.66	25(89.3)
18<Age≤65	M (40)	3.14 (±3.43)	2.43	0.20-16.96	29(72.5)
	F (43)	3.29 (±3.19)	1.98	0.01-15.51	31(72.1)
	83	3.22 (±3.31)	2.07	0.01-16.96	60(72.3)
Age>65	M (25)	3.87 (±3.82)	2.63	0.76-18.66	23(92.0)
	F (26)	2.23 (±1.71)	2.02	0.01-6.78	18(69.2)
	51	3.03 (±3.05)	2.30	0.01-18.66	41(80.4)
Total	199	3.96 (±4.20)	2.71	0.01-26.66	158(79.4)

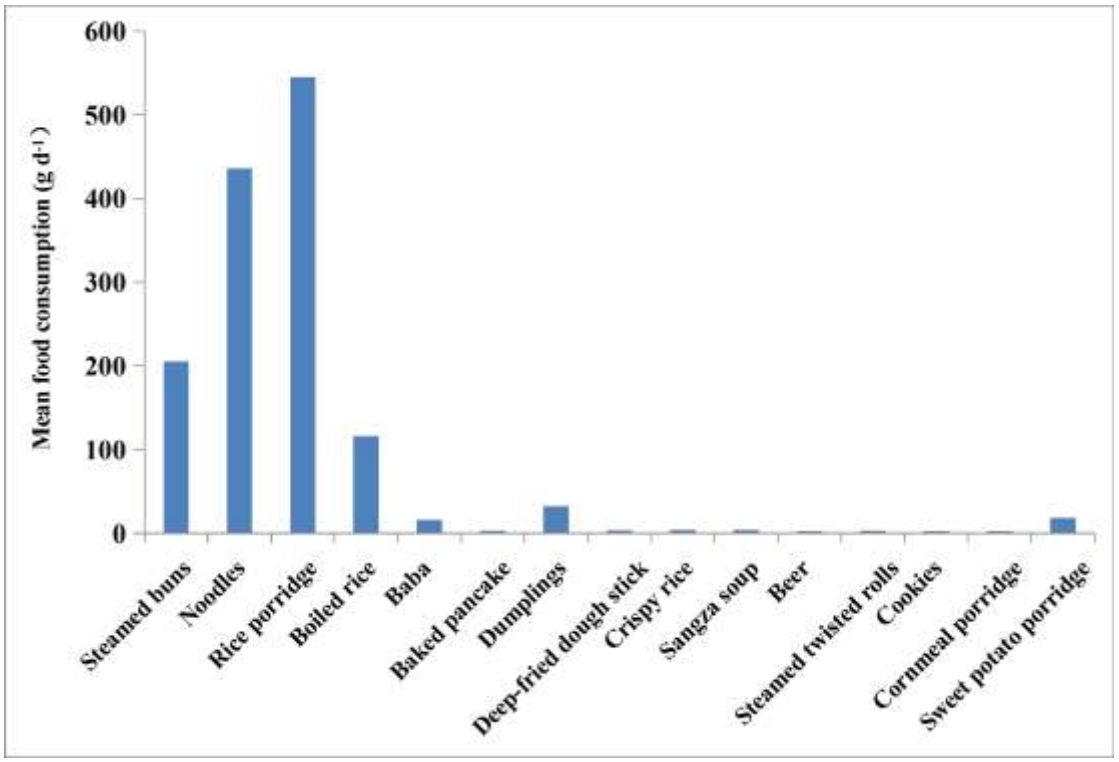
754

755 **Table 8** Comparison of dietary and internal exposure (μg kg^{-1} bw d^{-1})

	Percentiles (95%CI)					Exceeding
	Mean ± SD	P50	P75	P95	Range	PMTDI
EDI	2.54±1.63	2.19	3.36	6.01	0.16~9.78	171 (85.9%)
PDI with excretion rate correction	3.96±4.20	2.71	5.11	11.78	0.008~26.7	158 (79.4%)

756

757 **Figure 1**



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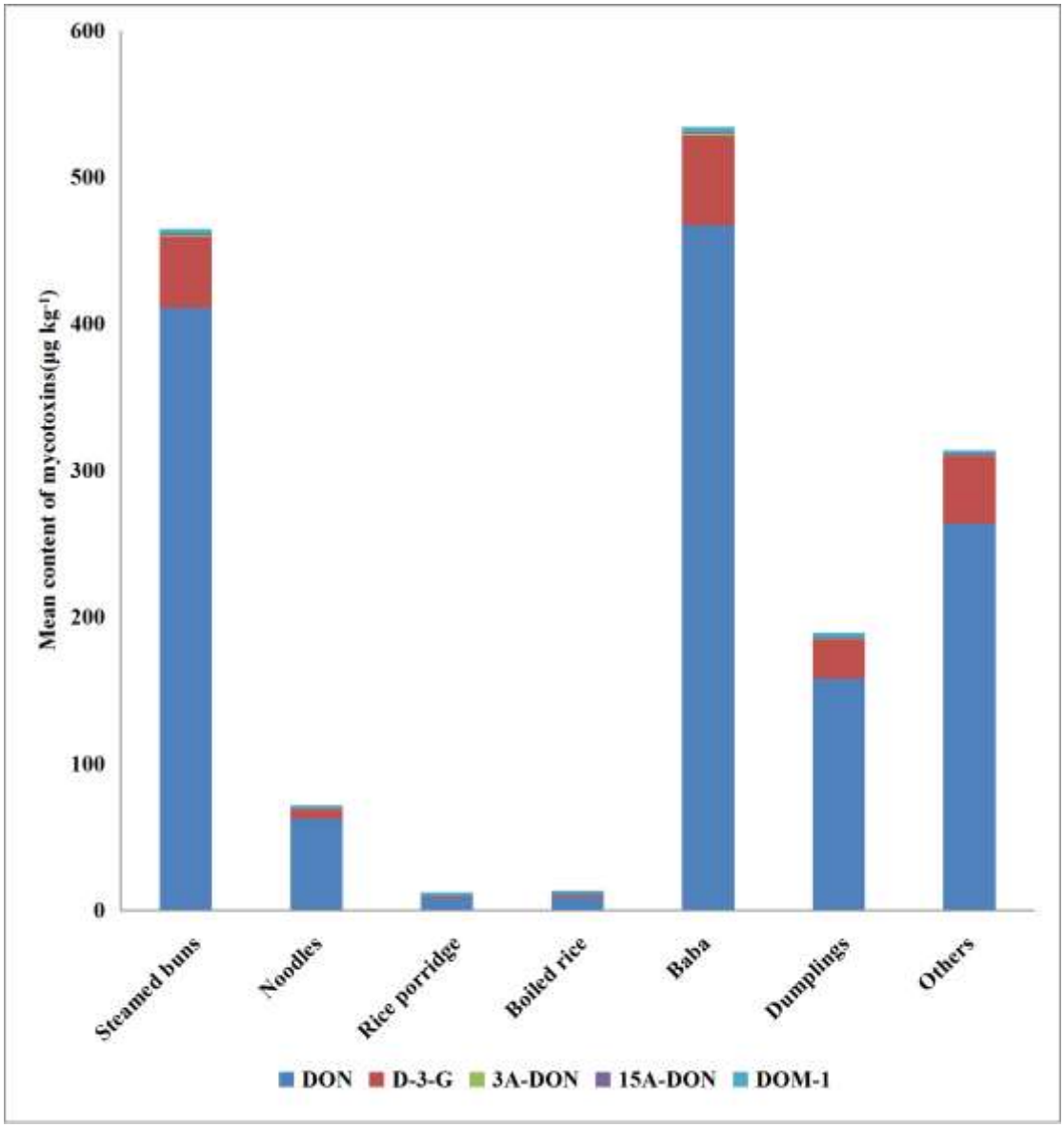
759

760 **Figure 2**

761



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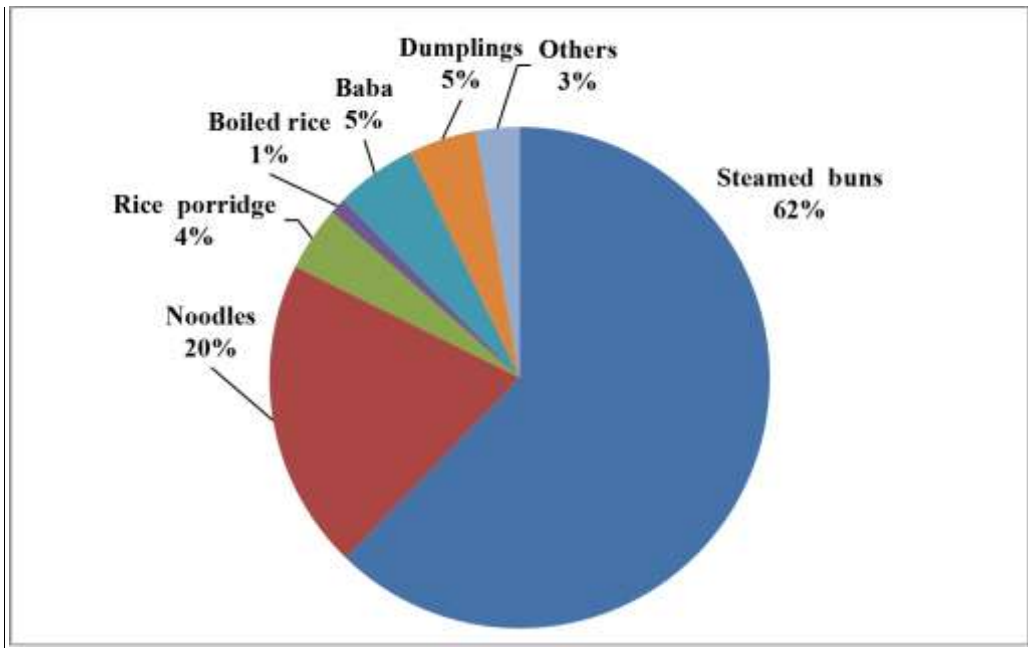
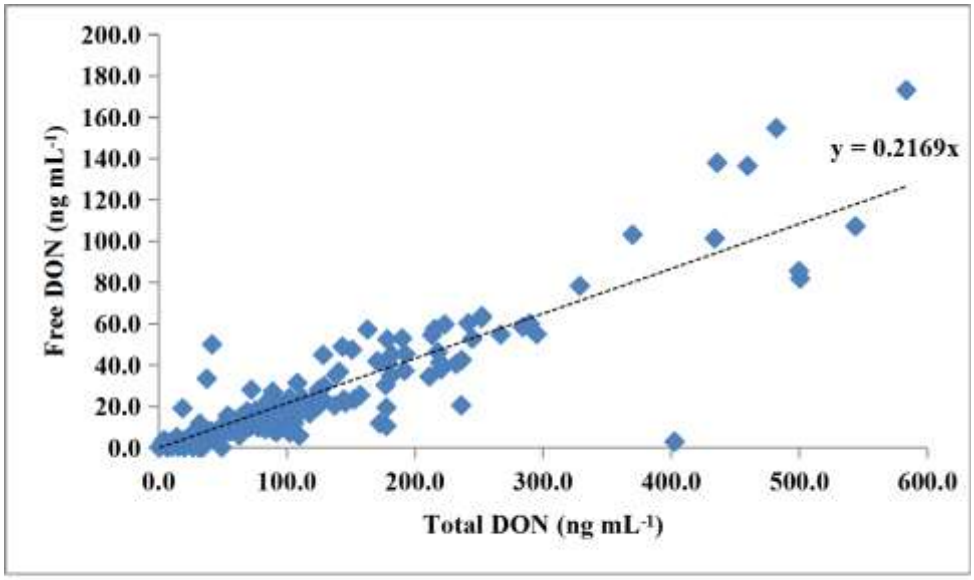
763

764 **Figure 3**

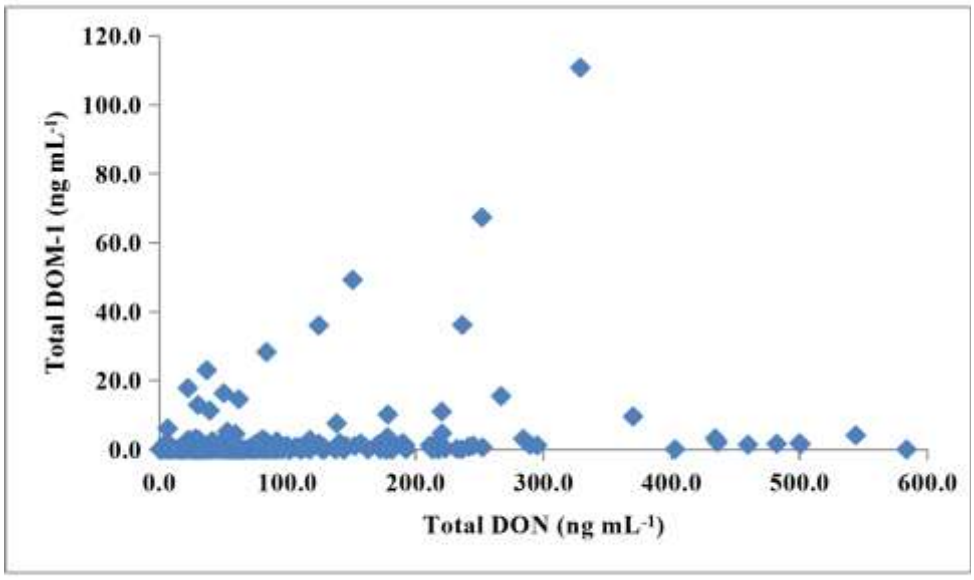


765

766 **Figure 4**



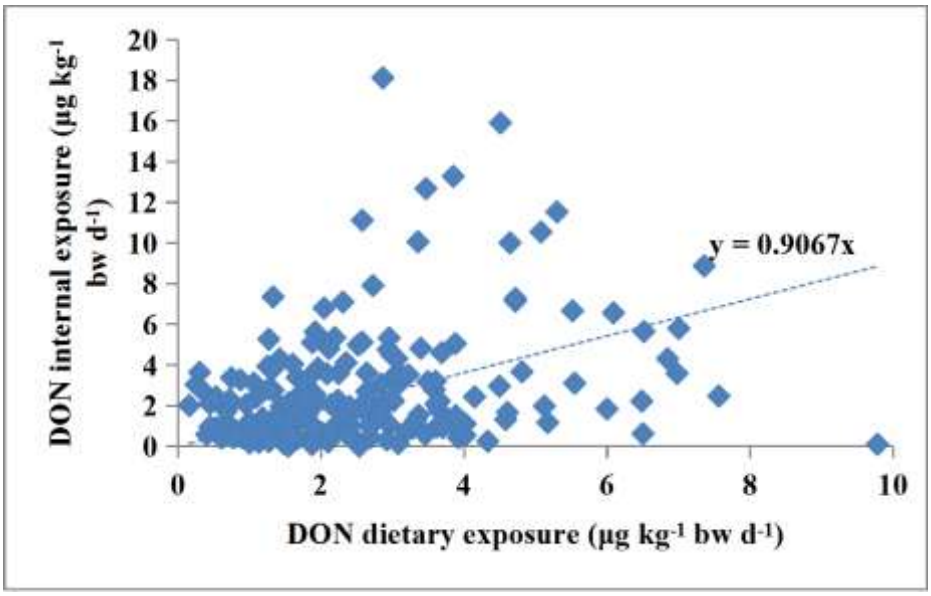
(a)



(b)

767

768 **Figure 5**



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