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Mycotoxins in cereals and cereal-based products: Incidence and probabilistic dietary risk assessment for the Brazilian population

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ABSTRACT

A probabilistic dietary risk assessment on mycotoxins was conducted using the Monte Carlo Risk Assessment software, with consumption data from the 2008/2009 Brazilian Household Budget Survey for individuals who were at least 10 years old and occurrence data for 646 samples of rice, maize, wheat, and their products, collected in the Federal District and in the state of Rio Grande do Sul, Brazil. Processing factors were estimated and applied to concentration data. Chronic exposure was estimated for fumonisins (free and bound/hidden), deoxynivalenol (DON) (including the acetylated forms) and zearalenone (ZON) (including alfa-zearalenol) and acute exposure was estimated for DON. For the general population, the chronic exposure exceeded the safe exposure levels at the 95P for DON and at the 99P for fumonisins. Additionally, safe level exceedance occurred at the 97.5P for fumonisins and at the 95P for DON for teenagers, as well as at the 99P for fumonisins for women of child-bearing-age. No exceedances were found for chronic exposure to ZON and acute exposure to DON. Maize couscous contributed most of the total fumonisins (91%) and ZON intakes (~40%) and bread to total intake of DON (~30%). Further studies should be conducted with updated Brazilian consumption data, which should include information for individuals aged less than 10 years old.

1. Introduction

Mycotoxins are toxic fungal metabolites that can contaminate food before and/or after harvesting (Frisvad et al., 2007; Kuiper-Goodman, 2004). The classes of mycotoxins that are most relevant to both human and animal health are aflatoxins and ochratoxin A, produced by *Aspergilus* sp., and fumonisins, trichothecenes and zearalenone produced by *Fusarium* sp. (Alshannaq and Yu, 2017; Lee and Ryu, 2017; Nicholson, 2004).

Aflatoxins (AFB1, AFB2, AFG1 and AFG2) are hepatotoxic, and they are classified as a human carcinogen by the International Agency for Research on Cancer (IARC, 1993). Aflatoxins are also immunotoxic agents, thus the exposure to them *in utero* and during early life causes negative effects on growth and development (JECFA, 2018). Fumonisin B1 (FB1) is classified as a probable human carcinogen (IARC, 2002), and fumonisin exposure has also been associated with neural tube defects, cardiovascular diseases and the prevalence of esophageal cancer (Kigen et al., 2017; Missmer et al., 2006; Ueno et al., 1997; Waes et al., 2005). Ochratoxin A (OTA), a possible human carcinogen (IARC, 1993), plays an important role in the pathogenesis of some renal diseases, including Balkan endemic nephropathy and kidney tumors that occur in certain endemic regions of the Balkan Peninsula, and chronic interstitial nephropathy occurring in Northern African countries (Malir et al., 2016). Deoxynivalenol (DON), a major mycotoxin from the trichothecene group, inhibits protein synthesis, impairs nutrient intake, affects hematopoiesis, induces neuro-endocrine effects, affects growth, reproduction and immune function after chronic exposure (Payros et al., 2016). At high doses, acute exposure to DON can cause abdominal pain, dizziness, headache, nausea and vomiting in pigs, dogs and cats (Pestka, 2010; JECFA, 2011), probably through activation of inflammatory

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pathways in intestinal epithelial cells (van de Walle et al., 2010). Emesis is indeed the most sensitive functional manifestation of DON acute toxicity in animals after oral exposure, and was the basis for the establishment of an acute reference dose (ARfD) for this mycotoxin (JECFA, 2011). Zearalenone (ZON) is known to cause estrogenic syndrome in pigs and is considered an endocrine disruptor in humans (Kowalska et al., 2016; Sherif et al., 2009).

Maize, rice, and wheat are cereals frequently consumed worldwide, and the occurrence of mycotoxins in these staple foods is widely documented (Alshannaq and Yu, 2017; Andrade and Caldas, 2015; Echodu et al., 2019; Lee and Ryu, 2017). Simultaneous exposure to mycotoxins is also an important issue that should be monitored (Lee and Ryu, 2017), as already pointed out by some authors regarding the synergistic effects of AFB1 and FB1 (Gelderblom et al., 2002; Meneely et al., 2018; Xiu et al., 2019). Various studies have evaluated the potential risks from the exposure to mycotoxins present in food around the world, using deterministic or probabilistic methods (Han et al., 2014; Mitchell et al., 2017; Assunção et al., 2018; Blanco-Lizarazo et al., 2019; Taghizadeh et al., 2020; JECFA, 2018). The probabilistic approach provides a more realistic exposure estimate of a given population compared to deterministic methods, as it considers the entire food consumption database and food concentration data (de Nijs et al., 2016).

Brazil is one of the main food producers in the world, with a wide range of agroclimatic zones (equatorial, tropical, subtropical, temperate and semiarid) that favor fungal growth and mycotoxin food contamination (Taniwaki et al., 2019). In Brazil, all the dietary exposure assessments with mycotoxins have been conducted using deterministic methods, and most have evaluated the exposure to only one mycotoxin in a specific region of the country, from the consumption of limited food commodities (Bordin et al., 2014; Caldas and Silva, 2007; Martins et al., 2012; Santos et al., 2013; Savi et al., 2016; Franco et al., 2019a).

The aims of this study were to evaluate the occurrence of aflatoxins, fumonisins, ochratoxin A, tricothecenes, zearalenone, citreoviridin, diacetoxyiscirpenol, and some metabolites in rice, maize, wheat, and their products; to estimate the dietary exposure of Brazilian consumers to the most prevalent mycotoxins through a probabilistic approach, and to assess the potential health risks arising from this exposure.

2. Materials and methods

2.1. Food consumption data

Brazilian consumption of maize, rice, and wheat-based products was obtained from the Brazilian Household Budget Survey (HBS; *Pesquisa de Orçamento Familiar* - POF 7) conducted by the Brazilian Institute of Geography and Statistics (IBGE) from July 2008 to June 2009 (the most recent data available in the country). The 2008/2009 HBS provided individual consumption data for 34,003 individuals from 10 to 104 years old (mean of 36.6 years ± 18.4) and with body weight from 19 to 150 kg (65.6 ± 15.6 kg). Data were obtained on two non-consecutive days, but not everyone filled out the two days of the survey. The total number of records (consumption days) was 67,704. Information about the composition of food-as-eaten (e.g. wheat flour in bread) was taken from different published sources (Araújo and Guerra, 2007; Fisberg and Slater Villar, 2002; Pinheiro, 2004), and well-known Brazilian food recipes from the internet. In total, consumption data for 93 foods-as-eaten that contained maize, rice, and wheat-based products were available in the 2008/2009 Brazilian HBS (Tables S1, S2 and S3; Supplementary Material). For the purpose of this study, maize flour and maize meal were considered together, except when specified otherwise. This was necessary because maize couscous and polenta, which are food widely consumed in Brazil, may be made using either maize flour or meal.

2.2. Samples analyzed

A total of 206 samples of maize, rice, and wheat-based food products were purchased from retail stores in Brasília (Federal District, Brazil) from May 2015 to February 2016. Products collected were maize starch (n = 6), degermed maize (*canjica*, n = 18), maize grits (*canjiquinha*; n = 3), breakfast cereal (n = 10), maize flour/meal (n = 28), popcorn (n = 13), maize snacks (n = 18), maize pasta (n = 1), rice (n = 39), rice flour (n = 3), rice pasta (n = 2), crackers (n = 14), wheat snacks (n = 6), wheat pasta (n = 30), and wheat flour (n = 15). At least 500 g/sample were collected, except for breakfast cereals, crackers and snacks (50 g minimum per sample). Samples were quartered, ground (blender), homogenized, sieved (18 mesh) and stored in polyethylene bags at room temperature until the analysis.

A total of 440 samples of maize flour/meal (n = 220) and wheat flour (n = 220) were purchased at retail stores in the cities of Cruz Alta and Santa Maria (Rio Grande do Sul, Brazil) from April 2013 to December 2014. Three individual 500 g packages of maize flour and three individual 1 kg packages of wheat flour were collected in order to compose 1 sample of each flour. All samples stayed at room temperature until they were analyzed.

2.3. Analytical methods

Samples collected in the Federal District were analyzed for aflatoxins (AFB1, AFB2, AFG1 and AFG2), citreoviridin (CTV), deoxynivalenol (DON), 15-acetyldeoxynivalenol (15AcDON), 3-acetyldeoxynivalenol (3AcDON), deoxynivalenol-3-glucoside (D3G), depoxy-deoxynivalenol (DOM), fumonisins (FB1, FB2 and FB3), fumonisin hydrolyzed forms (HFB1, HFB2 and HFB3), ochratoxin A (OTA), zearalenone (ZON), and alfa-zearalenol (α-ZOL) using a previously published method (Andrade et al., 2017). Briefly, a 5g sample was extracted with ACN:H_2O in the ultrasonic bath and centrifuged. Next, 1 mL of supernatant was evaporated, re-dissolved in MeOH:H_2O, 180 μL combined with 20 μL of the internal standard solution and injected in the LC-MS/MS. Samples were quantified using isotope labeled internal standards and matrix matched calibration curves. Three fortified samples were included in each extraction batch for internal quality control. LOQs for maize meal and derived products were: DON = 39.1 μg/kg; 15AcDON = 120.6 μg/kg; 3AcDON = 77.2 μg/kg; D3G = 60 μg/kg; DOM = 39.9 μg/kg; FB1 = 19.5 μg/kg; FB2 = 8 μg/kg; FB3 = 32 μg/kg; HFB1 = 6 μg/kg; ZON = 24.4 μg/kg; α-ZOL = 28 μg/kg. LOQs for wheat flour and derived products were: DON = 40.2 μg/kg; 15AcDON = 80.1 μg/kg; 3AcDON = 72.2 μg/kg; D3G = 61.3 μg/kg; DOM = 39.9 μg/kg; FB1 = 19.5 μg/kg; FB2 = 8 μg/kg; FB3 = 24 μg/kg; HFB1 = 8 μg/kg; ZON = 16 μg/kg; α-ZOL = 39.2 μg/kg. LOQs for rice and derived products: DON = 40 μg/kg; 15AcDON = 72 μg/kg; 3AcDON = 48 μg/kg; D3G = 60 μg/kg; DOM = 23.8 μg/kg; FB1 = 21.3 μg/kg; FB2 = 12 μg/kg; FB3 = 24 μg/kg; HFB1 = 8 μg/kg; ZON = 16 μg/kg; α-ZOL = 28 μg/kg (Andrade et al., 2017).

Bound/hidden fumonisins were determined as their hydrolyzed forms (HFB1, HFB2 and HFB3) and then converted to FB1, FB2 and FB3 using molar mass ratios, as described by Andrade et al. (2017). In summary, the sample was extracted using the previous procedure, lyophilized, submitted to basic hydrolysis at 60 °C to cleave non-extracted bound/hidden fumonisins, extracted with ACN, and the pH was adjusted to 3.0 ± 0.5. Tubes were sonicated, centrifuged, and stored in a freezer (−18 °C) for 12 h (solid-liquid extraction with low temperature purification). The liquid supernatant (organic phase) was filtered, evaporated under vacuum, the residues were dissolved in MeOH:H_2O and analyzed as previously described. Total fumonisin (FB1, FB2 and FB3) was expressed by the sum of the free fumonisins determined and the bound/hidden fumonisins. LOQs for bound/hidden fumonisins were defined as the LOQs for HFB1, HFB2 and HFB3, at 1.2, 1.8 and 2.5 μg/kg, respectively (Andrade et al., 2017).

A Shimadzu LC system (Shimadzu, Kyoto, Japan) coupled to a 4000

Qtrap triplequadrupole mass spectrometer (Sciex, Framingham, MA, USA), fitted with a Turbo Ion Spray electrospray ionization (ESI) source was used for LC-MS/MS analysis of samples collected in the Federal District. Chromatographic separation was performed at 40 °C, with a flow rate of 0.8 mL/min, using a Gemini C18 analytical column (150 × 4.6 mm, 5 μm) preceded by a C18 security guard cartridge (4.0 × 3.0 mm, 5 μm), both from Phenomenex® (Torrance, CA, USA). The elution was carried out with a gradient of water (A) and methanol (B), both containing 0.1% formic acid and 1 mM ammonium formate. ESI-MS/MS was done in the positive mode, using multiple reaction monitoring (MRM), scanning two fragmentation reactions per analyte (Andrade et al., 2017). The conditions of the mass spectrometer ion source were: entrance potential at 10V, ion source at 500 °C, ion source gas 1 and 2 at 50 (GS1) and 40 psi (GS2), ion spray voltage at 5500V, curtain gas at 12 psi, and collision gas at medium. Data acquisition and quantification were carried out using the software Analyst® (V 1.5.2). Additional details of the analytical method and the LC-MS/MS parameters were previously described (Andrade et al., 2017).

Samples collected in the state of Rio Grande do Sul were analyzed for aflatoxins, fumonisins (FB1 and FB2), DON, diacetoxyiscirpenol (DAS), OTA, T-2 and HT-2 toxins and ZON according to Reichert et al. (2018), with some modifications. Briefly, the slurry was prepared at a ratio of 1:1.5 (sample:water), 12.5 g were weighed into a falcon tube, 10 mL of acetonitrile (1% acetic acid) and 4.5 g of anhydrous magnesium sulfate were added, with agitation between each step, the tube was centrifuged, 0.5 mL of the supernatant transferred to a vial containing 0.5 mL of methanol, and 5 μL injected in a UPLC-MS/MS, using the partial loop with needle overfill mode. A Waters® UPLC-MS/MS system (Waters, USA) coupled to a Xevo TQ-S triple quadrupole mass spectrometer and an electrospray ionization (ESI) source was used for analysis. Chromatographic separation was performed at 60 °C, with a flow rate of 0.45 mL/min, using a BEH C18 analytical column (100 × 2.1 mm, 1.7 μm) from Waters® (Waters, USA). The mobile phase consisted of a gradient of water and acetonitrile, both acidified with 0.1% formic acid. ESI-MS/MS was done in the positive mode, using Z-spray interface, scanning two fragmentation reactions per analyte. The mass spectrometer ESI source parameters were: temperatures of the source at 100°, temperature of desolvation gas at 450 °C, desolvation gas flow rate at 600 L/h (N_2), cone gas flow rate at 100 L/h (N_2), capillary voltage at 2.5 kV, collision gas at 3.5 x 10^{-3}mbar (argon). Data acquisition and quantification were carried out using the software MassLynx® and TargetLynx® (V 4.1). Method accuracy and precision were satisfactory for all mycotoxins with recoveries between 70 and 120% and RSD ≤20% (n = 3) and samples were quantified using matrix matched calibration curves. LOQs for both maize and wheat flour were 1 μg/kg for AFB1, AFB2, AFG1, AFG2 and OTA; 50 μg/kg for FB1, FB2, DON, ZON, DAS and HT-2. For T-2, LOQs were 500 μg/kg for wheat flour and 50 μg/kg for maize flour. Additional details of the analytical method and the LC-MS/MS parameters were described by Reichert et al. (2018).

2.4. Processing factors

Samples of degermed maize (yellow and white), maize grits, maize meal, popcorn, wheat pasta and wheat flour, naturally contaminated with fumonisins, DON and/or ZON were submitted to processing procedures that mimic common household preparation in Brazil. Degermed maize and maize grits were separately cooked in water (under pressure) for 20 and 40 min, to prepare *canjica* and cooked grits (*canjiquinha*), respectively; maize meal was cooked in water for approximately 40 min to prepare *polenta,* and wheat pasta was cooked for 3–5 min. Popcorn was popped using a small amount of oil. Bread was prepared by mixing wheat flour, salt, saccharose, and baker's yeast with water in a bowl and then leaving it to rest (30 min). The dough was sliced, shaped, taken to the fermentation cabinet (4 h), and then baked for 18 min at 180 °C.

Processing factors (PFs) were estimated as the ratio of mycotoxin concentrations after (food-as-eaten) and before processing (food-as-analyzed). The PFs were then multiplied to the concentration found in all samples of degermed maize, maize grits, maize meal/flour, popcorn, pasta and wheat flour (food-as-analyzed) to estimate the concentration after processing (food-as-eaten).

2.5. Dietary risk assessment

Intakes were estimated using the Monte Carlo Risk Assessment software (MCRA, version 8.3), developed by Biometris, Wageningen University and Research Centre and the National Institute for Public Health and the Environment (RIVM) (de Boer et al., 2019; van der Voet et al., 2014).

MCRA offers several approaches to estimate chronic (usual) intake based on the consumption patterns of the dataset available. In this work, the Model-then-Add approach (MTA) was used to ensure that the intake estimated was modeled using the best fit for separate foods or food groups, avoiding erroneous intake estimates in the case of multimodal distributions (van der Voet et al., 2014). DON acute exposure was conducted using the Monte Carlo sampling approach, which multiplies a randomly selected daily consumption of food on a specific per-person day by a randomly chosen mycotoxin level per consumed food. The daily acute exposures per person-day were obtained by adding up all the exposures for each randomly selected person-day over the foods evaluated. The processing factors estimated in item 2.4 were applied in both models, and non-detected samples were assumed to be at ½ LOQ.

Exposures were estimated for the general population (10–114 years old) and for teenagers (12–18 years old) at the 90th, 95th, 97.5th, 99th and 99.9th percentiles (the highest for acute exposure to DON only). For total fumonisins, exposures were also estimated for women of child-bearing-age (12–45 years old), since these mycotoxins have been associated with the development of neural tube defects (Missmer et al., 2006; Waes et al., 2005).

The empirical bootstrap approach was used to estimate the uncertainty of the chronic and acute exposures due to the limited sample size of the food consumption and concentration data. In this approach, the dataset is resampled with a replacement to obtain a new set (or bootstrap sample) of the same size as the original. The two databases, both mycotoxin occurrence and food consumption, were resampled 100 times and the resulting databases were used to access the mycotoxin exposure for the Brazilian population.

The potential health risks from chronic exposure were evaluated by comparing the exposure percentiles with the provisional maximum tolerable daily intakes (PMTDI), which are 2 μg/kg bw for fumonisins (FB1, FB2, FB3 – alone or in combination; JECFA, 2001) and 1 μg/kg bw for DON (DON + 3AcDON + 15 AcDON; JECFA, 2001). For ZEA, the exposures were compared with the tolerable daily intake (TDI) of 0.25 μg/kg bw for zearalenone and its metabolites (including α-ZOL; EFSA, 2016). The potential health risks related to acute exposure to DON were evaluated by comparing the exposure percentiles with the acute reference dose (ARfD) of 8 μg/kg (DON + 3AcDON + 15 AcDON; JECFA, 2011). For the dietary exposure assessment, the LOQs inserted in MCRA were expressed as total fumonisins (free + bound/hidden FB1+FB2+FB3), total deoxynivalenol (DON + 3AcDON/15AcDON), and total zearalenone (ZON + α-ZOL), since the toxicological safety thresholds are established for the mycotoxin group. The LOQs were defined as the lowest LOQ among the individual mycotoxins in the group.

3. Results

3.1. Food consumption

A summary of consumption data (food-as-analyzed and food-as-eaten) for the relevant foods estimated from the 2008/2009 POF is shown in Table 1. Wheat flour has the highest number of food-as-eaten records (n = 68; Tables S2 and S3, Suplementary Material), reported in

Table 1
Summary of Brazilian individual consumption data obtained from the Brazilian Household Budget Survey (2008/2009 HBS) with individuals from 10 to 102 years old.

Food (n° of food-as-eaten)[a]	% of consumption days[b]	Mean consumption days (g)[c]	Main food-as-eaten
Maize flour/meal (10)	8.1	169	Maize couscous
Degermed maize[d] (2)	0.3	82.1	*Canjica*
Popcorn (1)	0.7	26.5	Popcorn
Maize starch (3)	0.0	200	Maize starch
Maize grits (1)	0.1	211	*Canjiquinha*
Breakfast cereals (1)	0.0	34.9	Breakfast cereals
Wheat flour (68)	24.3	58.3	Bread
Pasta (6)	8.6	163	Pasta
Crackers (1)	7.3	42.5	Crackers
Snacks (1)	0.6	101	Snacks

[a] Foods-as-eaten are listed in Table S1 (Supplementary Material), n = 92 (some preparations may include more than one food as analyzed).
[b] Related to the total number of consumption days (67,704).
[c] Mean consumption of the person-days at which the consumption of the food was reported.
[d] White and yellow

24.3% of consumption days, mainly as bread. Maize meal/flour products and pasta were reported in 8.1% (mean of 169 g) and 8.6% of consumption days (mean of 163 g), respectively. The highest mean consumption was found for products using maize grits (211 g) and maize starch (200 g), although the frequency of reporting was very low for these products (up to 0.1% of consumption days).

3.2. Mycotoxin occurrence

A total of 646 food samples were analyzed: 317 samples of maize products, 285 samples of wheat products, and 44 samples of rice and rice products. DON, FB1, FB2 and ZON were the most prevalent mycotoxins in the samples analyzed, and they were positive in 57.1, 48.1, 44.3 and 12.5% of the samples, respectively. Detailed data on mycotoxin occurrence are shown in the Supplementary Material (Table S4).

At least one fumonisin was found in all maize products, with FB1 and/or FB2 found in 89–92% of the 317 samples analyzed and FB3 in 23% of the 97 samples analyzed for this mycotoxin (Table S4). HFB1 was found in 14 samples of breakfast cereals, degermed maize, maize flour, maize meal, maize snacks, and popcorn (Table S4). DON was found in 96.5% of the wheat product samples analyzed, in 30% of the maize product samples, mainly maize flour (n = 89), and in one breakfast cereal, which was made of maize, rice, and wheat flour (Table S1). D3G was found in 20 samples, 60% of them cracker samples; 15AcDON was found only in a pre-cooked maize flour that also contained D3G and DON and in one sample of degermed white maize. ZON was found in 46 wheat products (16%), including all 14 cracker samples, in addition to 35 maize products, mainly maize flour (n = 27), and α-ZOL was found in only one sample of wheat snack.

Bound/hidden fumonisins were found in all 85 maize product samples analyzed for these forms, even in those without quantifiable amounts of the free forms, except for one breakfast cereal sample (Table 2). The levels of bound/hidden and total fumonisins (free forms + bound/hidden) are also shown in Table 2. On average, bound/hidden forms account for about 5% of total fumonisins, with the highest contribution found in maize pasta and maize flour (up to 16%).

Table 3 summarizes the occurrence data for total fumonisins, total DON (DON + acetylDON) and total zearalenone (ZON + α-ZOL), showing the means and the concentration ranges. The highest total fumonisin concentrations were found in maize flour (19,087 μg/kg), the highest total DON level in wheat flour (3,186 μg/kg) and highest total ZON level in maize flour (630 μg/kg). None of these mycotoxins were found at levels equal to or above the LOQ in maize starch and maize pasta samples; no zearalenone was found in breakfast cereal samples; and fumonisins were not found in crackers and wheat snacks. Fumonisins, DON and ZON were not found in rice and rice products.

The incidence of the other mycotoxins investigated in this study was low (Table S2). AFB1 was found in 27 samples, mainly maize flour (n = 25; range of 1–13 μg/kg), and AFB2 in five maize flour/meal samples (1–133 μg/kg) that also contained AFB1, and in one breakfast cereal sample. OTA was found in 8 samples (maize flour, pasta, breakfast

Table 2
Occurrence of bound/hidden fumonisins in maize-based products, and % of increase in total fumonisins caused by the presence of bound/hidden forms[a].

Products	N	Bound/hidden fumonisins Median (range), μg/kg	Total fumonisins Median (range), μg/kg	Increase in Total fumonisins[b] Median (range), %
Maize flour	18	4.8 (2.8–13.0)	380.2 (43.3–1051.7)	1.3 (0.6–16.2)
Maize meal	9	8.4 (3.8–29.9)	526.8 (328.7–1101)	1.6 (0.7–6.4)
Degermed maize	14	3.5 (2.7–8.4)	49.7 (26.6–1516.8)	4.7 (0.5–10.5)
Popcorn	13	5.0 (3.0–13.8)	197.2 (66.4–1042.2)	2.7 (0.8–10.6)
Maize starch	6	3.0 (2.9–3.7)	31.7 (31–32.8)	9.3 (8.7–11.2)
Maize grits	3	3.3 (2.7–3.7)	136.2 (68.5–136.3)	2.7 (2.4–3.9)
Breakfast cereals	5	3.3 (2.7–5.9)	92.3 (34.7–544.0)	4.5 (1.3–9.0)
Maize snacks	15	3.4 (3.0–10.7)	85.2 (39.3–303.5)	4.9 (1.2–9.5)
Maize pasta	1	9.4	59	16

[a] Only samples containing free fumonisins and bound/hidden fumonisins were considered.
[b] percentage of increase in total fumonisin content when the bound/hidden forms were added to the free forms.

Table 3
Total fumonisins, deoxynivalenol and zearalenone occurrence in maize and wheat product samples.

Products	N	Number of positive samples/mean of all samples[a] (range), μg/kg		
		Total fumonisins	Total deoxynivalenol	Total zearalenone
Maize flour/meal[b]	248	237/776.1 (<LOQ-19087)	89/58.2 (<LOQ-836.2)	27/31.9 (<LOQ -630)
Degermed maize	18	18/170.1 (2.7–1523)	2/28.4 (<LOQ -121)	2/13.9 (<LOQ -31.8)
Maize snacks	18	18/83.2 (2.9–303.5)	1/21.1 (<LOQ -40.4)	1/14.3 (<LOQ -54)
Popcorn	13	13/294.9 (28.3–1042.2)	1/26.6 (<LOQ -106.4)	3/20 (<LOQ -61.2)
Maize starch	6	6/31.7 (31–32.8)	0/<LOQ	0/<LOQ
Maize grits	3	3/113.7 (68.5–136.3)	1/44.5 (<LOQ -93.6)	2/21.5 (<LOQ -27.8)
Maize pasta	1	1/59 (59)	0/<LOQ	0/<LOQ
Breakfast cereals	10	10/72.8 (2.7–551.8)	1/30.1 (<LOQ -120.8)	0/<LOQ
Wheat flour	235	0/24 (4.0–25)	227/417.3 (<LOQ -3,186)	6/25 (<LOQ -79.2)
Wheat pasta	30	4/16.5 (<LOQ -130)	30/366.2 (83.9–860.8)	22/42.5 (<LOQ -205.6)
Crackers	14	0/<LOQ	14/560.7 (139.4–916.1)	14/60.7 (26.5–117.6)
Wheat snacks	6	0/<LOQ	4/255 (<LOQ -476.5)	4/75 (<LOQ -209.2)

N: number of samples analyzed; [a] Samples below LOQ were replaced by ½ LOQ to estimate the mean; LOQs for total mycotoxins were defined as the lowest LOQ of each group; [b] Includes products with different grinding sizes and that may have been submitted to thermal treatment; Total fumonisins = free + bound/hidden FB1+FB2+FB3; Total deoxinivalenol = DON +3AcDON/15AcDON; Total zearalenone = ZON + αZOL; Rice samples were not showed in this table since there was no positive sample detected.

cereals, and maize snacks) and CTV was found in 5 rice grain samples (19.8–3472 μg/kg) and in one cracker sample at a very high level (8,640 μg/kg). T-2 and α-ZOL were found in only two samples (maize flour and wheat snack). AFG1, AFG2, DAS, 3AcDON, DOM and HT-2 were not found in any sample analyzed.

3.3. Processing factors

Unprocessed and processed commodities were analyzed, and the estimated processing factors are shown in Table 4. Fumonisins were not found in some samples of cooked degermed maize (FB1, n = 2; FB2, n = 1) and popped popcorn (FB2, n = 3). ZON was not found in processed wheat pasta after cooking. Median (best estimate) processing factors were below 1 in all cases, indicating a decrease in mycotoxin concentration after processing.

3.4. Dietary risk assessment for total fumonisins, total DON and total ZON

The incidences of aflatoxins, OTA, CVT, T2/HT2, in the samples analyzed were low and no assessments were conducted for these mycotoxins. Chronic exposure was evaluated for total fumonisins, total DON and total ZON and acute exposure for total DON, the only mycotoxin with an ARfD established.

Table 5 shows the chronic dietary exposure assessment for total fumonisins, total DON and total ZON for the Brazilian population at the various percentiles of exposures and the 95% confidence intervals (between 2.5% and 97.5% percentiles of the uncertainty interval). For total fumonisins, the MTA model that showed the best fit of the Q-Q plots modeled maize flour, snacks and pasta separately using logistic Normal-Normal (LNN), and the remaining foods (n = 7) using observed individual means (OIM). This approach was used for all population subsets. For the general population and for women of child-bearing-age, the mean intake exceeded the PMTDI of 2 μg/kg bw at the 99P of exposure (122 and 105%, respectively). For teenagers, exceedance occurred at the 97.5P (106%). The consumption of maize couscous, a Brazilian dish prepared from maize flour or meal, contributed to about 90% of the total exposure for all the population subsets (Fig. 1).

For total DON, the best fit of the MTA Q-Q plots was found by modeling maize flour, degermed maize, popcorn, pasta, and wheat flour using LNN, and the remaining foods (n = 5) with OIM. The mean chronic intake exceeded the PMTDI (1 μg/kg bw) for the general population at the 99P of exposure (126%) and for teenagers at the 95P (104%) (Table 5). The consumption of different types of bread contributed to about 30% of the total DON intake, followed by pasta (17–21%) and crackers (16%) (Fig. 1).

The best fit of the MTA Q-Q plots for ZON was found after modeling degermed maize, wheat flour, popcorn and maize flour with LNN, and the remaining foods (n = 5) with OIM. The mean chronic intake did not exceed the TDI for any of the percentiles evaluated (Table 5), and the consumption of maize couscous, bread and crackers contributed to 16–31% of the total exposure for both subpopulations (Fig. 1).

The mean acute intake for total DON reached 4.86 μg/kg bw at the 99.9P for the general population and 6.35 μg/kg bw for teenagers (Table 6), below the ARfD of 8 μg/kg bw, even when considering the upper limit of the confidence interval (7.51 μg/kg bw for teenagers). Bread, pasta, and crackers were the foods that most contributed to DON acute exposure, accounting for about 70% of the total intake (Fig. 2).

Table 4
Processing factors (PF) obtained from naturally contaminated samples, used to estimate concentration of fumonisins, total deoxynivalenol (DON) and zearalenone (ZON).

Food	Processing	Mycotoxin	Number of trials[a]	PF	
				Range	Median
Maize meal	Cooking	Fumonisins	6	0.85–1.48	0.98
Degermed maize	Cooking	Fumonisins	5	<LOQ-0.69	0.33
Popcorn	Popping	Fumonisins	8	<LOQ-1.38	0.27
Maize grits	Cooking	Fumonisins	2	0.72–0.97	0.84
Wheat flour	Baking	DON	2	0.89–0.97	0.93
Wheat pasta	Cooking	DON	10	0.47–0.86	0.56
		ZON	1	<LOQ	<LOQ

[a] Number of samples analyzed before and after processing.

4. Discussion

This study included contamination data for mycotoxins in 646 food samples (rice and rice products, maize products, and wheat products) collected in the Federal District, which is in the Midwest region of Brazil and where Brasilia, the capital of the country is located, and in Rio Grande do Sul state (RS), in the Southern region of the country. RS is responsible for about 90, 87, and 21% of wheat, rice, and maize national production, respectively (CONAB, 2019). Levels of fumonisins found in the samples did not exceed the current Brazilian maximum limit (ML) of 1500 μg/kg (Brazil, 2011), except for one sample of degermed maize (1523 μg/kg), and only a whole-wheat pasta sample exceeded the ML for ZON (205.6 μg/kg; ML = 200 μg/kg). For DON (ML = 750 μg/kg), 19 maize flour samples (836.2–19,087 μg/kg), and 30 wheat flour samples were above the legal level (804–3186 μg/kg). No sample exceeded the ML established for aflatoxins in cereals and their products (Brazil, 2011).

In general, there is a low prevalence of mycotoxins in rice samples collected in Brazil (Almeida et al., 2012; Carvalho et al., 2010; Dors et al., 2011; Franco et al., 2019a; Katsurayama et al., 2018; Savi et al., 2018; Silva et al., 2019), but the incidence of aflatoxins in some Asian and Middle Eastern countries is high (Ali, 2019; Taghizadeh et al., 2020). In the present study, only CVT was detected in the 39 rice samples analyzed, at levels ranging from 19.8 to 3472 μg/kg (Table S1). The incidence (12.8%) and the levels are much higher than the only two studies that analyzed CVT in Brazilian rice (up to 6%; 0.9–254 μg/kg), both related to samples collected in the region of a beriberi outbreak that occurred in the country in 2007–2009 (Rosa et al., 2010; Almeida et al., 2012). These results indicate the need to further investigate this mycotoxin in the country. CVT is an ATP synthase inhibitor and one of the etiology factors of cardiac beriberi and Keshan disease (Feng et al., 2019).

Fusarium verticillioides and *Fusarium proliferatum*, the main fumonisin producers, are known to be the most common pathogens in maize (*Zea mays*) (Marasas, 2001), and high prevalence of these mycotoxins in maize and maize products is expected. Indeed, all maize-based product samples analyzed had at least one fumonisin present, with a mean level of 518.4 μg/kg (FB1+FB2+FB3). High prevalence of fumonisins in maize-based products was also reported in other studies in Brazil (Andrade et al., 2018; Barroso et al., 2017; Bordin et al., 2014; Bordini et al., 2019; Caldas and Silva, 2007; Franco et al., 2019b; Martins et al., 2012) and elsewhere (see the review by Lee and Ryu, 2017). In this study, fumonisins were also found in breakfast cereals not exclusively made of maize (up to 386 μg/kg FB1) and in wheat pasta (up to 67.6 μg/kg FB1; Table S2).

Fumonisins can covalently or non-covalently bind to matrix food constituents, mainly during thermal processes, and may not be extracted during the usual analytical methods, which can underestimate the dietary human exposure to these mycotoxins (Dall'Asta et al., 2008; Berthiller et al., 2013). In this study, bound/hidden fumonisins accounted for up to 16% of total fumonisin concentration, lower than what was found in other studies (Dall'Asta et al., 2009, 2008; Park et al., 2004; Hu et al., 2019). Oliveira et al. (2015) showed that hidden fumonisins (not covalently bound to maize components) in maize grain corresponded to 1.5–3.8 times the concentration of free fumonisins (FB1 and FB2).

Fusarium graminearum is a major pathogen in wheat, causing the Fusarium head blight disease that affects wheat production worldwide;

Table 5
Chronic dietary risk assessment of total fumonisins, total deoxynivalenol and total zearalenone for the Brazilian population.

Percentile	Total fumonisins PMTDI = 2 μg/kg bw per day[a]		Total deoxynivalenol PMTDI = 1 μg/kg bw per day[b]		Total zearalenone PMTDI = 0.25 μg/kg bw per day[c]	
	Mean intake[d] (CI)	%PMTDI[e]	Mean intake[d] (CI)	%PMTDI[e]	Mean intake[d] (CI)	%PMTDI[e]
General population (10–102 years)						
Mean	0.07 (0.06–0.09)	4	0.05 (0.05–0.06)	5	0.005 (0.004–0.006)	2
90	0.39 (0.33–0.49)	19	0.54 (0.50–0.58)	54	0.05 (0.04–0.05)	20
95	0.91 (0.77–1.14)	46	0.74 (0.68–0.80)	74	0.07 (0.06–0.08)	28
97.5	1.51 (1.27–1.88)	76	0.96 (0.89–1.04)	96	0.10 (0.09–0.11)	40
99	2.44 (2.04–3.08)	122	1.26 (1.17–1.36)	126	0.15 (0.13–0.16)	60
Teenagers (12–18 years)						
Mean	0.1 (0.08–0.12)	5	0.09 (0.77–0.10)	9	0.008 (0.007–0.01)	3
90	0.62 (0.45–0.82)	31	0.77 (0.70–0.84)	77	0.07 (0.07–0.08)	28
95	1.28 (1.02–1.69)	64	1.04 (0.93–1.13)	104	0.10 (0.09–0.12)	40
97.5	2.11 (1.61–2.78)	106	1.25 (1.16–1.35)	125	0.14 (0.12–0.16)	56
99	3.17 (2.37–4.22)	159	1.60 (1.42–1.76)	160	0.18 (0.16–0.21)	72
Women of child-bearing-age (12–45 years)						
Mean	0.08 (0.07–0.1)	4	–	–	–	–
90	0.38 (0.30–0.47)	19	–	–	–	–
95	0.83 (0.67–1.01)	42	–	–	–	–
97.5	1.39 (1.14–1.73)	70	–	–	–	–
99	2.09 (1.71–2.62)	105	–	–	–	–

[a] FB1 + FB2+ FB3; JECFA, 2001.
[b] DON +3 acetyl DON +15 acetyl DON; JECFA, 2001.
[c] Include metabolites; EFSA, 2016.
[d] In μg/kg bw per day. CI = lower (LL, 2.5%) - upper (UL, 97.5%) limits at 95% confidence interval.
[e] Rounded up to 3 significant figures.

the fungus is also the main producer of trichothecenes (Khan et al., 2020). In this study, 96% of the wheat flour (53–3186 μg/kg), all wheat pasta (84.0–861 μg/kg) and cracker (139.4–916.1 μg/kg) samples contained DON (Table S2). High levels and incidence of DON were also found in some studies in the country (Almeida et al., 2016; Lanza et al., 2019), while in others the incidences were lower (35–58%; Machado et al., 2017; Rocha et al., 2017; Savi et al., 2016). In China, over 70% of the wheat flour and maize flour contained DON (Sun and Wu, 2016), while less than 40% of the maize flour samples analyzed in the present study contained this mycotoxin. In general, the occurrence of ZON in wheat and wheat flour available in Brazil is low (Lanza et al., 2019; Tralamazza et al., 2016), but both the level of contamination and the percentage of positive samples may change significantly over the years (Mallmann et al., 2017). In this study, about 10% of the maize flour samples contained ZON, and although the incidence in wheat flour was low (2.5%), 73% of the wheat pasta and all cracker samples contained this mycotoxin. The occurrence of DON and ZON in maize and its products has also been reported in other studies in Brazil (Oliveira et al., 2017; Pante et al., 2019).

AFB1 is a genotoxic compound, and constant monitoring of its levels in cereals and continuous action by health authorities to decrease aflatoxin exposure are necessary (JECFA, 2018). Jager et al. (2016) found that 57% of the 28 samples of maize flour collected in the state of São Paulo contained AFB1, and up to 40% of the rice samples analyzed in other studies conducted in Brazil had aflatoxins (Katsurayama and Taniwaki, 2017; Katsurayama et al., 2018). However, data presented in this paper showed a low incidence of AFs, which were present only in maize flour (10.5% contained AFB1), in one sample of maize snacks, and in one sample of rice pasta.

To avoid high uncertainties in the probabilistic exposure assessment due to the large number of censored data (<LOQ) for aflatoxins, OTA, CVT, DAS, HT2 and T-2, the exposure assessments and the potential risks to Brazilian consumers were estimated only for fumonisins (free and bound/hidden), DON (including its acetylated forms) and ZON (including α-ZOL), which had the highest incidence of positive samples. The chronic exposure to fumonisins exceeded the PMTDI only at higher percentiles (at the 99P for the general population and women of child-bearing-age, at the 97.5P for teenagers), with consumption of maize couscous accounting for most of the total intake for all population subsets evaluated. Chronic exposure to DON exceeded the PMDI at the 99P for general population and the 95P for teenagers, with bread, pasta and crackers, all wheat-based products, contributing the most to the total DON intake. The mean exposure to ZON and the acute exposure to DON did not exceed the safe exposure level, even at the highest percentiles of the intake distributions for both populations. One challenge for risk management authorities when evaluating the results of a risk assessment is to identify the level of exposure that should raise a health concern and require actions to decrease the exposure. For mycotoxins, the 95P has been used as the chronic exposure level of concern to drive management actions, and higher percentiles may be considered for acute exposure (Marin et al., 2013; EFSA, 2014). The European Food Safety Authority (EFSA) used the 95P of exposure to evaluate the safety of the maximum levels of deoxynivalenol (DON), fumonisins and zearalenone (ZON) in maize and maize products in the region (EFSA, 2014).

All the chronic dietary risk assessment studies conducted in the country for fumonisins, DON and ZON used the deterministic approach to estimate exposure, but most included only a few food products and analyzed samples and were limited to certain Brazilian regions; only one considered the consumption of food-as-eaten (such as bread), and none included bound fumonisins, and DON and ZON metabolites. Most assessments did not find any risk to humans from the chronic exposure. Although a direct comparison with the results obtained in present study is limited, some published studies will be discussed here.

Bordin et al. (2014) estimated a FB1 intake of 0.06 μg/kg bw for a São Paulo state city population using concentration data from 129 maize product samples and consumption data obtained from a Food Frequency Questionnaire collected from 39 residents. Savi et al. (2016) estimated a similar fumonisin intake level (0.07 μg/kg bw) by the Santa Catarina State population from the consumption of milled maize and maize-based products using data from the 2008/2009 HBS (mean availability of each food in the household). Using the same consumption data, Bordini et al. (2019) estimated a fumonisin (FB1+FB2) intake of 0.096 μg/kg by the Brazilian population, using concentration data in maize endosperm, maize meal and maize grits. Using the individual consumption data from the 2008/2009 HBS, Andrade et al. (2018) estimated that the intake of fumonisins (FB1+FB2+FB2) through the consumption of popcorn ranged from 0.0051 μg/kg bw (lower bound; <LOD = 0) to 0.1943 μg/kg bw (upper bound; <LOD = LOD) for total population and from 4.85 to 26.9 μg/kg bw for high consumers. This last approach overestimates the risks from chronic exposure to fumonisins, as it is unlikely

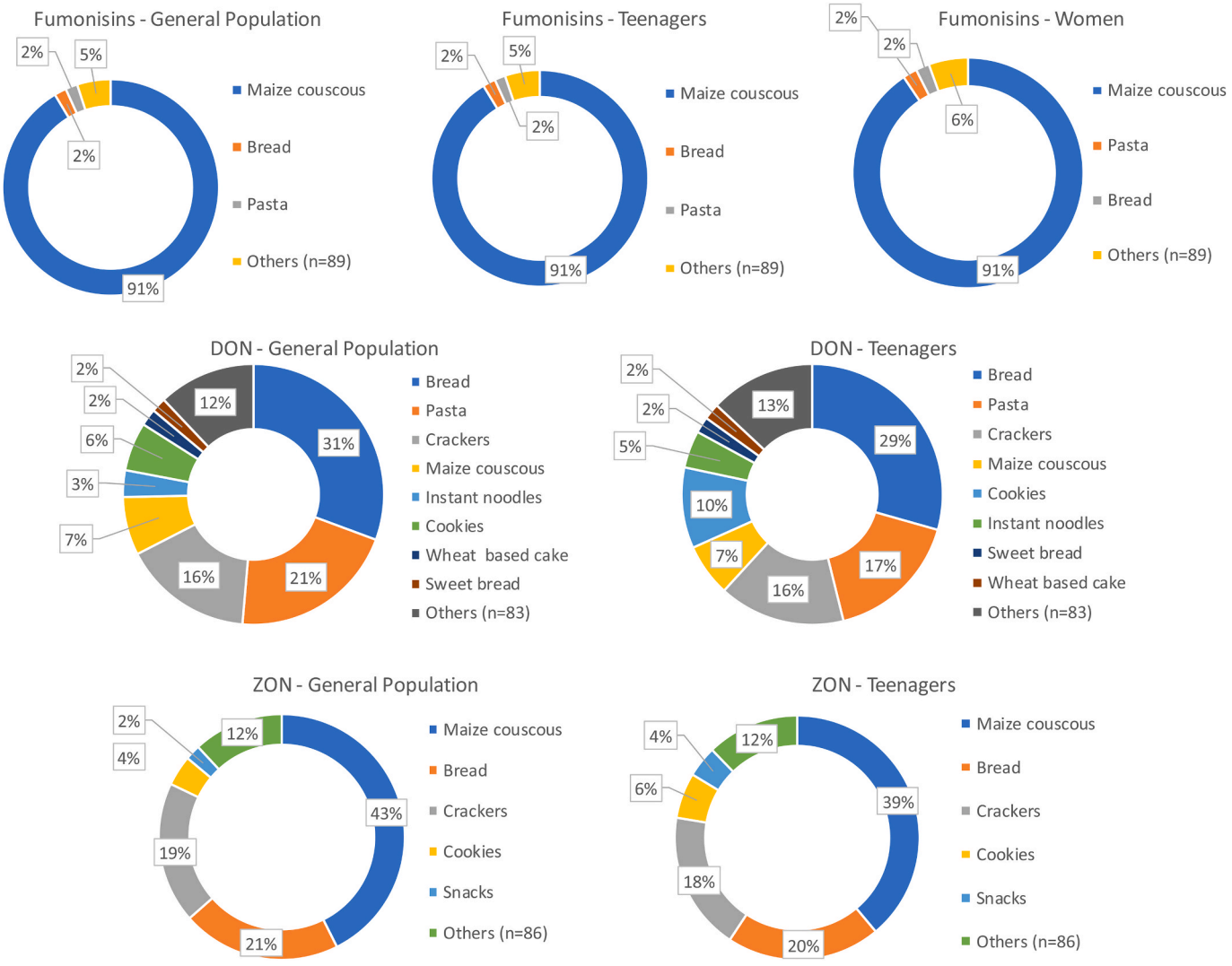

Fig. 1. Food categories that most contributed to chronic intake of fumonisins, deoxynivalenol and zearalenone. Cookies include *biscoito recheado* (biscuits with cream filling) and *biscoito doce* (sweet biscuits); Full description of foods grouped into the category 'others' can be found in the Supplementary Material (Table S3).

Table 6
Acute dietary exposure assessment of total deoxynivalenol (ARfD = 8 μg/kg bw) for the Brazilian population.

Percentile	General population (10–102 years)		Teenagers (12–18 years)	
	Intake (CI)	% ARfD	Intake (CI)	% ARfD*
90	0.61 (0.55–0.65)	8	0.88 (0.81–0.94)	11
95	1.03 (0.94–1.12)	13	1.43 (1.30–1.53)	18
97.5	1.55 (1.40–1.69)	19	2.08 (1.87–2.29)	26
99	2.33 (2.10–2.63)	29	3.06 (2.71–3.40)	38
99.9	4.86 (3.94–6.0)	61	6.35 (4.87–7.51)	79

CI = lower (LL, 2.5%) - upper (UL, 97.5%) limits at 95% confidence interval; * rounded up to 2 significant figures.

that an individual would be a high consumer of popcorn on a daily basis. In the present study, the consumption of popcorn accounted for only 0.2% of the total dietary fumonisin intake.

Savi et al. (2016) evaluated the exposure of the Southern Brazilian population to DON through the consumption of wheat-based products (food availability from the 2008/2009 HBS) and samples collected in Santa Catarina State, showing that the estimated intake did not exceed the PMTDI even when the highest consumption data was used. In the study conducted by Silva et al. (2018), 172 wheat flour samples in Paraná State were analyzed for DON and the amount of wheat flour in the products was estimated, assuming that wheat flour is 9.8% protein. The DON intake by the Brazilian population ranged from 0.31 μg/kg bw for elderly males to 0.62 μg/kg bw for female teenagers, below the PMTDI.

The exposure of the Brazilian population to ZON through the consumption of maize meal samples collected in the state of Paraná, Brazil (food availability from the 2008/2009 HBS) estimated by Pante et al. (2019) ranged from 1.6 ng/kg bw day (Midwest region; upper level) to 6.4 ng/kg bw day (Northwest; upper level). Franco et al. (2019a) assessed the exposure of residents from rural areas of São Paulo and Santa Catarina states to multiple mycotoxins using two different approaches: the direct (analysis of biomarkers in urine samples) and the indirect (24 h dietary recall and occurrence data on rice, beans, wheat flour, maize flour and maize meal). The two approaches gave different results, with the daily intake estimated from the biomarkers exceeding the TDI for ZON and the PMTDI for OTA, and the daily intake estimated through the consumption exceeding the PMTDI for DON, which agrees with our results using consumption data. Exposure to mycotoxins is primarily dietary, and it is possible that the inconsistency found between the two approaches is related to the uncertainty of the consumption data (Franco et al., 2019a).

Dietary exposure to mycotoxins has also been assessed in various

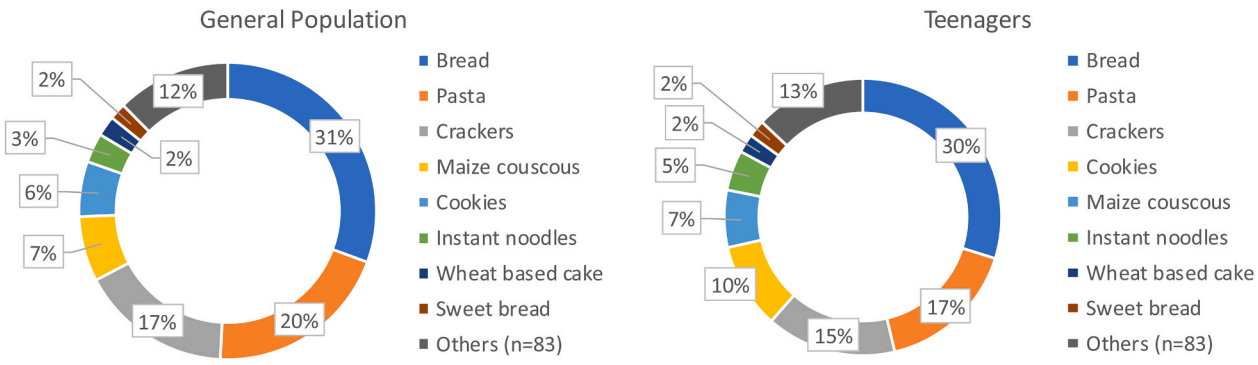

Fig. 2. -Food categories that most contributed to total acute intake of deoxynivalenol.

other countries. De Boevre et al. (2013) evaluated human exposure to trichothecenes, ZON, metabolites and their hidden forms through the consumption of cereal-based foods in Belgium, using both deterministic and probabilistic approaches. The authors concluded that, although the intake for most of the Belgian population did not exceed the safe exposure levels for DON, ZEN and the sum of T-2 and HT-2, there is a large subpopulation exceeding those safety values. The probabilistic dietary risk assessment conducted by Sun and Wu (2016) in China considering the consumption of a range of cereals showed that the intake for total DON exceeded the PMTDI at the 99P (3.5 μg/kg bw day). The probabilistic exposure to DON through the consumption of bread by the Hungarian population was estimated by Ambrus et al. (2011) and showed that the intake exceeded the PMTDI in 5–15% of the cases, depending on the approach used. The authors found that health risks may be present at lower percentiles (from the 85P) for chronic exposure and at the 99.9P for acute exposure, which is a worse situation than what was found in the present study for the Brazilian population, considering other food contributors in the exposure.

The intake estimations and the assessed risks reported in this study have uncertainties that are inherent to dietary exposure risk assessments. Uncertainties in the exposure assessment are related to the limited sample size for concentration and/or food consumption and can be decreased if more data are made available (Kettler et al., 2015; Tenant et al., 2017). In this study, these uncertainties were quantified by the bootstrap approach, and reported as 95% confidence intervals (between the 2.5% and 97.5% percentiles of the uncertainty interval) around the percentiles of exposure. The highest percentiles have larger uncertainties than moderate ones, since they are based on fewer data points. Additional uncertainties can be assessed qualitatively. Uncertainties in the concentration data are related primarily to the sampling procedure, which in this study was limited to two Brazilian regions, the uncertainty inherent to the analytical method and the uncertainty related to the PFs applied to the concentration data, which in some cases were estimated based on only a few trials. Uncertainties related to food consumption in this study were mostly due to the extrapolation of the food consumption data obtained during the years of 2008–2009 for the years that the samples were collected for analysis (2013–2016), and the conversion of foods/ingredients (food-as-eaten) to their food-as-analyzed counterparts, which were obtained mainly from reference books. Finally, uncertainties on the risk characterization are related to the toxicological data and on how the reference doses (PMTDI, TDI or ARfD) were derived, a process that occurs during the hazard characterization of the risk assessment process. Traditionally, the reference doses are estimated by dividing the NOAEL (No Observed Adverse Effect Level) obtained in animal studies by a safety factor to extrapolate to humans, both values having a great degree of uncertainty (WHO, 2018; Chiu et al., 2018). A probabilistic approach to estimate reference doses has been proposed (WHO, 2018). Using DON as an example, the degree of uncertainty was estimated as 200, i.e., the true target human dose (HD) could be considered 200 times higher than the probabilistic estimated reference dose (WHO, 2018).

To the best of our knowledge, this is the first study to conduct a probabilistic dietary assessment to evaluate the exposure of the Brazilian population to mycotoxins. The study included metabolites and bound/hidden forms in the assessment, although their contribution to the total mycotoxins was low. Furthermore, the intake considered the consumption of all food prepared with wheat and maize flour for which consumption data are available and used processing factors to refine the assessment. However, the study has two major limitations that should be commented on. A small number of rice samples were analyzed, which may have hampered the detection of the investigated mycotoxins in this cereal. Rice is a staple food in the Brazilian diet and dietary exposure assessment to mycotoxins through its consumption is essential in the country. Furthermore, the individual consumption data available for the Brazilian population do not include children under 10 years, a population that has a higher consumption rate per body weight than adults for some foods and therefore a higher exposure level. In a study conducted with Portuguese children (one to three years old), a potential adverse health effect from aflatoxin exposure through the consumption of cereal products was found at intake percentiles of 50P or higher (Assunção et al., 2018). Using urinary biomarkers, Gratz et al. (2019) showed that children in the United Kingdom were frequently exposed to levels of DON and OTA exceeding the tolerable daily intake (52 and 95% of cases, respectively).

5. Conclusion

The probabilistic dietary risk assessment to mycotoxins in Brazil showed that the chronic intake only exceeds the safe exposure level at the 95P of the intake distribution for DON (teenagers; 104% of the PMTDI). This information could be used as a guide for future management decisions by government authorities. Exposure to DON was mainly due to contamination of wheat flour and consumption of bread and pasta). Maize couscous, widely consumed by the Brazilian population, was the food that most contributed to fumonisin and zearalenone intakes.

This was a very extensive risk assessment study that covered a large range of cereal-derived foods that are potentially a source of mycotoxin exposure, but new studies should be conducted when more recent consumption data for the Brazilian population are available. These data should include information for individuals younger than 10 years old. Human biomonitoring studies linked with food surveys and health studies are also necessary to contribute to a more accurate assessment of the Brazilian population's exposure to mycotoxins.

Fusarium species infect maize and wheat grains and produce DON, fumonisins and zearalenone mainly at the pre-harvesting stage. Various strategies could be used to decrease mycotoxin contamination and minimize the potential health effects on consumers. Farmers in Brazil, as well in other countries, should apply good agricultural practices, including controlling insect damage and fungal infection with pest

management program and using hybrids adapted to environmental stresses that favor fungal growth. Additionally, Brazilian government should periodically revise its legislation concerning maximum limits for mycotoxins, in addition to a continuous surveillance of mycotoxins in grain and cereal-based products.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Patrícia Diniz Andrade: Conceptualization, Methodology, Validation, Formal analysis, Writing - original draft. **Jonatan Vinicius Dias:** Methodology, Formal analysis. **Darliana Mello Souza:** Methodology, Formal analysis. **Alessandra Page Brito:** Formal analysis. **Gerda van Donkersgoed:** Software, Data curation. **Ionara Regina Pizzutti:** Methodology, Validation, Funding acquisition, Writing - review & editing. **Eloisa Dutra Caldas:** Conceptualization, Funding acquisition, Supervision, Project administration, Data curation, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fct.2020.111572.

References

Ali, N., 2019. Aflatoxins in rice: worldwide occurrence and public health perspectives. Toxicol Rep 6, 1188–1197. https://doi.org/10.1016/j.toxrep.2019.11.007.

Almeida, A.P. de, Lamardo, L.C.A., Shundo, L., Silva, S.A. da, Navas, S.A., Alaburda, J., Ruvieri, V., Sabino, M., 2016. Occurrence of deoxynivalenol in wheat flour, instant noodle and biscuits commercialised in Brazil. Food Addit. Contam. Part B Surveill. 29 (4), 482–489. https://doi.org/10.1080/19393210.2016.1195880.

Almeida, M.I., Almeida, N.G., Carvalho, K.L., Gonçalves, G.A.A., Silva, C.N., Santos, E.A., Garcia, J.C., Vargas, E.A., 2012. Co-occurrence of aflatoxins B_1, B_2, G_1 and G_2, ochratoxin A, zearalenone, deoxynivalenol, and citreoviridin in rice in Brazil. Food Addit. Contam. Part A. Chem. Anal. Control. Expo. Risk Assess. 29, 694–703. https://doi.org/10.1080/19440049.2011.651750.

Alshannaq, A., Yu, J.H., 2017. Occurrence, toxicity, and analysis of major mycotoxins in food. Int. J. Environ. Res. Publ. Health 14 (632), 1–20. https://doi.org/10.3390/ijerph14060632.

Ambrus, Á., Szeitzne-Szabó, M., Zentai, A., Sali, J., Szabó, I.J., 2011. Exposure of consumers to deoxynivalenol from consumption of white bread in Hungary. Food Addit. Contam. Part A Chem. Anal. Control. Expo. Risk Assess. 28 (2), 209–217. https://doi.org/10.1080/19440049.2010.540720.

Andrade, G.C.R.M., Pimpinato, R.F., Francisco, J.G., Monteiro, S.H., Calori-Domingues, M.A., Tornisielo, V.L., 2018. Evaluation of mycotoxins and their estimated daily intake in popcorn and cornflakes using LC-MS techniques. Lebensm. Wiss. Technol. 95, 240–246. https://doi.org/10.1016/j.lwt.2018.04.073.

Andrade, P.D., Caldas, E.D., 2015. Aflatoxins in cereals: worldwide occurrence and dietary risk assessment. World Mycotoxin J. 8 (4), 415–431. https://doi.org/10.3920/WMJ2014.1847.

Andrade, P.D., Dantas, R.R., Moura-Alves, T.L.D.S.D., Caldas, E.D., 2017. Determination of multi-mycotoxins in cereals and of total fumonisins in maize products using isotope labeled internal standard and liquid chromatography/tandem mass spectrometry with positive ionization. J. Chromatogr., A 1490, 138–147. https://doi.org/10.1016/j.chroma.2017.02.027.

Araújo, M.O., Guerra, T.M., 2007. In: Alimentos Per Capita, 3 Ed. Ed. Universitária-UFRN.

Assunção, R., Martins, C., Vasco, E., Jager, A., Oliveira, C., Cunha, S.C., Fernandes, J.O., Nunes, B., Loureiro, S., Alvito, P., 2018. Portuguese children dietary exposure to multiple mycotoxins - an overview of risk assessment under MYCOMIX project. Food Chem. Toxicol. 118, 399–408. https://doi.org/10.1016/j.fct.2018.05.040.

Blanco-Lizarazo, C.M., Gamboa-Marín, A., Vega, S., Jiménez-Rodríguez, L.P., Sánchez B, I.C., 2019. Assessment of dietary exposure to aflatoxin B_1 from corn arepas in Colombia. Food Addit. Contam. Part A, Chemistry, analysis, control, exposure & risk assessment 36 (7), 1109–1117. https://doi.org/10.1080/19440049.2019.1615643.

Barroso, V.M., Rocha, L.O., Reis, T.A., Reis, G.M., Duarte, A.P., Michelotto, M.D., Correa, B., 2017. Fusarium verticillioides and fumonisin contamination in Bt and non-Bt maize cultivated in Brazil. Mycotoxin Res. 33, 121–127. https://doi.org/10.1007/s12550-017-0271-4.

Berthiller, F., Crews, C., Dall'Asta, C., Saeger, S.D., Haesaert, G., Karlovsky, P., Oswald, I. P., Seefelder, W., Speijers, G., Stroka, J., 2013. Masked mycotoxins: a review. Mol. Nutr. Food Res. 57 (1), 165–186. https://doi.org/10.1002/mnfr.201100764.

Bordin, K., Rosim, R.E., Neeff, D.V., Rottinghaus, G.E., Oliveira, C.A.F., 2014. Assessment of dietary intake of fumonisin B1 in São Paulo, Brazil. Food Chem. 155, 174–178. https://doi.org/10.1016/j.foodchem.2014.01.057.

Bordini, J.G., Ono, M.A., Hirozawa, M.T., Garcia, G.T., Vizoni, E., Ono, E.Y.S., 2019. Safety of corn and corn-based products intended for human consumption concerning fumonisins from a brazilian processing plant. Toxins 11 (33), 1–11. https://doi.org/10.3390/toxins11010033.

Brazil, 2011. Aprova o Regulamento Técnico Sobre Limites Máximos Tolerados (LMT) para micotoxinas em alimentos, Diário Oficial da União – D.O.U., de 22 de fevereiro de 2011. http://portal.anvisa.gov.br/documents/33916/393845/Resolu%25C3%25A7%25C3%25A3o%2B0-2011-GGALI.pdf/21b70cd7-1465-4c7c-a348-20a38df86945 accessed 05 April 2020.

Caldas, E.D., Silva, A.C.S., 2007. Mycotoxins in corn-based food products consumed in Brazil: an exposure assessment for fumonisins. J. Agric. Food Chem. 55 (19), 7974–7980. https://doi.org/10.1021/jf0712898.

Carvalho, R.A. de, Batista, L.R., Prado, G., Oliveira, B.R. de, Silva, D.M. da, 2010. [Incidência de fungos toxigênicos e aflatoxinas em arroz]. Cienc. Agroteciência e Agrotecnologia 34, 946–952. https://doi.org/10.1590/S1413-70542010000400021.

Chiu, W.A., Axelrad, D.A., Dalaijamts, C., Dockins, C., Shao, K., Shapiro, A.J., Paoli, G., 2018. Beyond the RfD: broad application of a probabilistic approach to improve chemical dose-response assessments for noncancer effects. Environ. Health Perspect. 126 (6), 067009 https://doi.org/10.1289/EHP3368.

CONAB (Companhia Brasileira de Abastecimento, 2019. V. 6 - SAFRA 2018/19- N. 12. https://aprosojabrasil.com.br/wp-content/uploads/2019/09/BoletimZGraosZsetembroZ-ZresumoZ2019.pdf. accessed 05 April 2020.

Dall'Asta, C., Galaverna, G., Aureli, G., Dossena, Aa, Marchelli, R., 2008. A LC/MS/MS method for the simultaneous quantification of free and masked fumonisins in maize and maize-based products. World Mycotoxin J. 1, 237–246. https://doi.org/10.3920/WMJ2008.x040.

Dall'Asta, C., Galaverna, G., Mangia, M., Sforza, S., Dossena, A., Marchelli, R., 2009. Free and bound fumonisins in gluten-free food products. Mol. Nutr. Food Res. 53, 492–499. https://doi.org/10.1002/mnfr.200800088.

De Boer, W.J., Goedhart, P.W., Hart, A., Kennedy, M.C., Kruisselbrink, J., Owen, H., Roelofs, W., van der Voet, H., 2019. MCRA 8.3. A web-based program for Monte Carlo Risk Assessment. Reference Manual.

De Boevre, M., Jacxsens, L., Lachat, C., Eeckhout, M., Di Mavungu, J.D., Audenaert, K., Maene, P., Haesaert, G., Kolsteren, P., De Meulenaer, B., De Saeger, S., 2013. Human exposure to mycotoxins and their masked forms through cereal-based foods in Belgium. Toxicol. Lett. 218 (3), 281–292. https://doi.org/10.1016/j.toxlet.2013.02.016.

De Nijs, M., Mengelers, M.J.B., Boon, P.E., Heyndrickx, E., Hoogenboom, L.A.P., Lopez, P., Mol, H.G.J., 2016. Strategies for estimating human exposure to mycotoxins via food. World Mycotoxin J. 9 (5), 831–845. https://doi.org/10.3920/WMJ2016.2045.

Dors, G.C., Bierhals, V. da S., Badiale-Furlong, E., 2011. Parboiled rice: chemical composition and the occurrence of mycotoxins. Ciência Tecnol. Aliment. 31 (1), 172–177. https://doi.org/10.1590/S0101-20612011000100025.

Echodu, R., Maxwell Malinga, G., Moriku Kaducu, J., Ovuga, E., Haesaert, G., 2019. Prevalence of aflatoxin, ochratoxin and deoxynivalenol in cereal grains in northern Uganda: Implication for food safety and health. Toxicol. Reports 6, 1012–1017. https://doi.org/10.1016/j.toxrep.2019.09.002.

EFSA (European Food Safety Agency), 2016. Appropriateness to set a group health-based guidance value for zearalenone and its modified forms. EFSA Panel on Contaminants in the Food Chain (CONTAM). EFSA Journal 14 (4), 4425. https://doi.org/10.2903/j.efsa.2016.4425.

EFSA (European Food Safety Authority), 2014. Evaluation of the increase of risk for public health related to a possible temporary derogation from the maximum level of deoxynivalenol, zearalenone and fumonisins for maize and maize products. EFSA Panel on Contaminants in the Food Chain (CONTAM). EFSA Journal 12 (5), 3699. https://doi.org/10.2903/j.efsa.2014.3699.

Feng, C., Li, D., Chen, M., Jiang, L., Liu, X., Li, Q., Geng, C., Sun, X., Yang, G., Zhang, L., Yao, X., 2019. Citreoviridin induces myocardial apoptosis through PPAR-γ-mTORC2-mediated autophagic pathway and the protective effect of thiamine and selenium. Chem. Biol. Interact. 311, 108795. https://doi.org/10.1016/j.cbi.2019.108795.

Fisberg, R.M., Slater Villar, B., 2002. Manual de receitas e medidas caseiras para cálculo de inquéritos alimentares: manual elaborado para auxiliar o processamento de dados de inquéritos alimentares.

Franco, L.T., Petta, T., Rottinghaus, G.E., Bordin, K., Gomes, G.A., Alvito, P., Assunção, R., Oliveira, C.A.F., 2019a. Assessment of mycotoxin exposure and risk characterization using occurrence data in foods and urinary biomarkers in Brazil. Food Chem. Toxicol. 128, 21–34. https://doi.org/10.1016/j.fct.2019.03.046.

Franco, L.T., Petta, T., Rottinghaus, G.E., Bordin, K., Gomes, G.A., Oliveira, C.A.F., 2019b. Co-occurrence of mycotoxins in maize food and maize-based feed from small-

scale farms in Brazil: a pilot study. Mycotoxin Res. 35 (1), 65–73. https://doi.org/10.1007/s12550-018-0331-4.
Frisvad, J.C., Thrane, U., Samson, R.A., 2007. Mycotoxin producers. In: Dijksterhuis, J., Samson, R.A. (Eds.), Food Mycology: A Multifaceted Approach to Fungi and Food. CRC Press, Boca Raton. https://doi.org/10.1201/9781420020984.
Gelderblom, W.C.A., Marasas, W.F.O., Lebepe-Mazur, S., Swanevelder, S., Vessey, C.J., De la M Hall, P., 2002. Interaction of fumonisin B1 and aflatoxin B1 in a short-term carcinogenesis model in rat liver. Toxicology 171 (2–3), 161–173. https://doi.org/10.1016/S0300-483X(01)00573-X.
Gratz, S.W., Currie, V., Duncan, G., Jackson, D., 2020. Multimycotoxin exposure assessment in UK children using urinary biomarkers-A pilot survey. J. Agric. Food Chem. 68 (1), 351–357. https://doi.org/10.1021/acs.jafc.9b03964.
Han, Z., Nie, D., Ediage, E.N., Yang, X., Wang, J., Chen, B., Li, S., On, S.L., De Saeger, S., Wu, A., 2014. Cumulative health risk assessment of co-occurring mycotoxins of deoxynivalenol and its acetyl derivatives in wheat and maize: case study, Shanghai, China. Food Chem. Toxicol. 74, 334–342. https://doi.org/10.1016/j.fct.2014.10.018.
Hu, L., Liu, H., Yang, J., Wang, C., Wang, Y., Yang, Y., Chen, X., 2019. Free and hidden fumonisins in raw maize and maize-based products from China. Food Addit. Contam. Part B Surveill 12 (2), 90–96. https://doi.org/10.1080/19393210.2018.1564371.
IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2002. Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. IARC Monogr. Eval. Carcinog. Risks Hum. 82, 1–556. PMID: 12687954; PMCID: PMC4781602.
IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, 1993. Some naturally occurring substances: food items and constituents, heterocyclic aromatic amines and mycotoxins. IARC Monogr. Eval. Carcinog. Risks Hum. 56, 1–599.
Jager, A.V., Tonin, F.G., Baptista, G.Z., Souto, P.C.M.C., Oliveira, C.A.F., 2016. Assessment of aflatoxin exposure using serum and urinary biomarkers in São Paulo, Brazil: a pilot study. Int. J. Hyg Environ. Health 219 (3), 294–300. https://doi.org/10.1016/j.ijheh.2015.12.003.
JECFA, 2001. Evaluation of Certain Mycotoxins in Food: Fifty-Sixth Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, 906. World Health Organization, Geneva, Switzerland.
JECFA, 2011. Evaluation of Certain Contaminants in Food: Seventy-Second Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, vol. 959. World Health Organization, Rome, Italy.
JECFA, 2018. Evaluation of Certain Contaminants in Food: Eighty-Third Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, vol. 1002. World Health Organization, Geneva, Switzerland.
Katsurayama, A.M., Martins, L.M., Iamanaka, B.T., Fungaro, M.H.P., Silva, J.J., Frisvad, J.C., Pitt, J.I., Taniwaki, M.H., 2018. Occurrence of Aspergillus section Flavi and aflatoxins in Brazilian rice: from field to market. Int. J. Food Microbiol. 2 (266), 213–221. https://doi.org/10.1016/j.ijfoodmicro.2017.12.008.
Katsurayama, A.M., Taniwaki, M.H., 2017. Fungi and aflatoxins in rice: occurrence and significance to consumer health. Braz. J. Food Technol. 20, e2017006 https://doi.org/10.1590/1981-6723.0617.
Kettler, S., Kennedy, M., McNamara, C., Oberdörfer, R., O'Mahony, C., Schnabel, J., Smith, B., Sprong, C., Faludi, R., Tennant, D., 2015. Assessing and reporting uncertainties in dietary exposure analysis: mapping of uncertainties in a tiered approach. Food Chem. Toxicol. 82, 79–95. https://doi.org/10.1016/j.fct.2015.04.007.
Khan, M.K., Pandey, A., Athar, T., et al., 2020. Fusarium head blight in wheat: contemporary status and molecular approaches. 3 Biotech 10, 172. https://doi.org/10.1007/s13205-020-2158-x.
Kigen, G., Busakhala, N., Kamuren, Z., Rono, H., Kimalat, W., Njiru, E., 2017. Factors associated with the high prevalence of oesophageal cancer in Western Kenya: a review. Infect. Agents Canc. 12 (59), 1–11. https://doi.org/10.1186/s13027-017-0169-y.
Kowalska, K., Habrowska-Górczyńska, D.E., Piastowska-Ciesielska, A.W., 2016. Zearalenone as an endocrine disruptor in humans. Environ. Toxicol. Pharmacol. 48, 141–149. https://doi.org/10.1016/j.etap.2016.10.015.
Kuiper-Goodman, T., 2004. Risk assessment and risk management of mycotoxins in food. In: Magan, N., Olsen, M. (Eds.), Mycotoxins in Food. Woodhead Publishing Limited, Cambridge, England, pp. 3–31.
Lanza, A., da Silva, R.C., dos Santos, I.D., Pizzutti, I.R., Cence, K., Cansian, R.L., Zeni, J., Valduga, E., 2019. Mycotoxins' evaluation in wheat flours used in Brazilian bakeries. Food Sci. Biotechnol. 28, 931–937. https://doi.org/10.1007/s10068-018-0537-4.
Lee, H.J., Ryu, D., 2017. Worldwide occurrence of mycotoxins in cereals and cereal-derived food products: public health perspectives of their Co-occurrence. J. Agric. Food Chem. 65 (33), 7034–7051. https://doi.org/10.1021/acs.jafc.6b04847.
Machado, L.V., Mallmann, C.A., Mallmann, A.O., Coelho, R.D., Copetti, M.V., 2017. Deoxynivalenol in wheat and wheat products from a harvest affected by fusarium head blight. Food Sci. Technol. 37 (1), 8–12. https://doi.org/10.1590/1678-457X.05915.
Malir, F., Ostry, V., Pfohl-Leszkowicz, A., Malir, J., Toman, J., 2016. Ochratoxin A: 50 years of research. Toxins 8 (191), 1–49. https://doi.org/10.3390/toxins8070191.
Mallmann, C.A., Dilkin, P., Mallmann, A.O., Oliveira, M.S., Adaniya, Z.N.C., Tonini, C., 2017. Prevalence and levels of deoxynivalenol and zearalenone in commercial barley and wheat grain produced in Southern Brazil: an eight-year (2008 to 2015) summary. Trop. Plant Pathol. 42, 146–152. https://doi.org/10.1007/s40858-017-0152-6.
Marasas, W.F., 2001. Discovery and occurrence of the fumonisins: a historical perspective. Environ. Health Perspect. 109 (Suppl. 2), 239–243. https://doi.org/10.1289/ehp.01109s2239.
Marin, S., Ramos, A.J., Cano-Sancho, G., Sanchis, V., 2013. Mycotoxins: occurrence, toxicology, and exposure assessment. Food Chem. Toxicol. 260, 218–237. https://doi.org/10.1016/j.fct.2013.07.047.
Martins, F.A., Ferreira, F.M.D., Ferreira, F.D., Bando, É., Nerilo, S.B., Hirooka, E.Y., Machinski, M., 2012. Daily intake estimates of fumonisins in corn-based food products in the population of Parana, Brazil. Food Contr. 26 (2), 614–618. https://doi.org/10.1016/j.foodcont.2012.02.019.
Mitchell, N.J., Chen, C., Palumbo, J.D., Bianchini, A., Cappozzo, J., Stratton, J., Ryu, D., Wu, F., 2017. A risk assessment of dietary Ochratoxin a in the United States. Food Chem. Toxicol. 100, 265–273. https://doi.org/10.1016/j.fct.2016.12.037.
Meneely, J.P, Hajslová, J., Krska, R., Elliott, C.T., 2018. Assessing the combined toxicity of the natural toxins, aflatoxin B_1, fumonisin B_1 and microcystin-LR by high content analysis. Food Chem. Toxicol. 121, 527–540. https://doi.org/10.1016/j.fct.2018.09.052.
Missmer, S.A., Suarez, L., Felkner, M., Wang, E., Merrill, A.H., Rothman, K.J., Hendricks, K.A., 2006. Exposure to fumonisins and the occurrence of neural tube defects along the Texas-Mexico border. Environ. Health Perspect. 114 (2), 237–241. https://doi.org/10.1289/ehp.8221.
Nicholson, P., 2004. Rapid detection of mycotoxigenic fungi in plants. In: Magan, N., Olsen, M. (Eds.), Mycotoxins in Food. Woodhead Publishing Limited, Cambridge, England, pp. 111–136.
de Oliveira, G.B., de Castro Gomes Vieira, C.M.C.G., Orlando, R.M., Faria, A.F., 2017. Simultaneous determination of fumonisins B1 and B2 in different types of maize by matrix solid phase dispersion and HPLC-MS/MS. Food Chem. 233, 11–19. https://doi.org/10.1016/j.foodchem.2017.04.091.
Oliveira, M.S., Diel, A.C.L., Rauber, R.H., Fontoura, F.P., Mallmann, A., Dilkin, P., Mallmann, C.A., 2015. Free and hidden fumonisins in Brazilian raw maize samples. Food Contr. 53, 217–221. https://doi.org/10.1016/j.foodcont.2014.12.038.
Pante, G.C., Silva, M.V., Romoli, J.C.Z., Rocha, G.H.O., Bando, E., Nerilo, S.B., Mossini, S.A.G., Machinski, M., 2019. Occurrence of zearalenone in corn meal commercialized in south region of Brazil and daily intake estimates in the Brazilian population. J. Food Saf. 39, e12672 https://doi.org/10.1111/jfs.12672.
Park, J.W., Scott, P.M., Lau, B.P., Lewis, D.A., 2004. Analysis of Heat-Processed Corn Foods for Fumonisins and Bound Fumonisins, vol. 21, pp. 1168–1178. https://doi.org/10.1080/02652030400021873.
Payros, D., Alassane-Kpembi, I., Pierron, A., Loiseau, N., Pinton, P., Oswald, I.P., 2016. Toxicology of deoxynivalenol and its acetylated and modified forms. Arch. Toxicol. 90 (12), 2931–2957. https://doi.org/10.1007/s00204-016-1826-4.
Pestka, J.J., 2010. Deoxynivalenol: mechanisms of action, human exposure, and toxicological relevance. Arch. Toxicol. 84, 663–679. https://doi.org/10.1007/s00204-010-0579-8.
Pinheiro, A.B.V., 2004. Tabela Para Avaliação de Consumo Alimentar em Medidas Caseiras - Livraria Livro Vivo | Estante Virtual.
Reichert, B., de Kok, A., Pizzutti, I.R., Scholten, J., Cardoso, C.D., Spanjer, M., 2018. Simultaneous determination of 117 pesticides and 30 mycotoxins in raw coffee, without clean-up, by LC-ESI-MS/MS analysis. Anal. Chim. Acta 1004, 40–50. https://doi.org/10.1016/j.aca.2017.11.077.
Rocha, D.F. de L., Oliveira, M., dos, S., Furlong, E.B., Junges, A., Paroul, N., Valduga, E., Backes, G.T., Zeni, J., Cansian, R.L., 2017. Evaluation of the TLC quantification method and occurrence of deoxynivalenol in wheat flour of southern Brazil. Food Addit. Contam. Part A Chem. Anal. Control. Expo. Risk Assess. 34 (12), 2220–2229. https://doi.org/10.1080/19440049.2017.1364872.
Rosa, C.A.R., Keller, K.M., Oliveira, A.A., Almeida, T.X., Keller, L.A.M., Marassi, A.C., Kruger, C.D., Deveza, M.V., Monteiro, B.S., Nunes, L.M.T., Astoreca, A., Cavaglieri, L.R., Direito, G.M., Eifert, E.C., Lima, T.A.S., Modernell, K.G., Nunes, F.I. B., Garcia, A.M., Luz, M.S., Oliveira, D.C.N., 2010. Production of citreoviridin by Penicillium citreonigrum strains associated with rice consumption and beriberi cases in the Maranhão State, Brazil. Food Addit. Contam. Part A. Chem. Anal. Control. Expo. Risk Assess. 27 (2), 241–248. https://doi.org/10.1080/19440040903289712, 27, 241.
Santos, J.S. Dos, Souza, T.M., Ono, E.Y.S., Hashimoto, E.H., Bassoi, M.C., Miranda, M.Z. De, Itano, E.N., Kawamura, O., Hirooka, E.Y., 2013. Natural occurrence of deoxynivalenol in wheat from Paraná State, Brazil and estimated daily intake by wheat products. Food Chem. 138, 90–95. https://doi.org/10.1016/j.foodchem.2012.09.100.
Savi, G.D., Piacentini, K.C., Rocha, L.O., Carnielli-Queiroz, L., Furtado, B.G., Scussel, R., Zanoni, E.T., Machado-de-Ávila, R.A., Corrêa, B., Angioletto, E., 2018. Incidence of toxigenic fungi and zearalenone in rice grains from Brazil. Int. J. Food Microbiol. 270 (2), 5–13. https://doi.org/10.1016/j.ijfoodmicro.2018.02.004.
Savi, G.D., Piacentini, K.C., Tibola, C.S., Santos, K., Sousa Maria, G., Scussel, V.M., 2016. Deoxynivalenol in the wheat milling process and wheat-based products and daily intake estimates for the Southern Brazilian population. Food Contr. 62, 231–236. https://doi.org/10.1016/j.foodcont.2015.10.029.
Sherif, S.O., Salama, E.E., Abdel-Wahhab, M.A., 2009. Mycotoxins and child health: the need for health risk assessment. Int. J. Hyg Environ. Health 212, 347–368. https://doi.org/10.1016/j.ijheh.2008.08.002.
Silva, L.P. da, Madureira, F., de Azevedo Vargas, E., Faria, A.F., Augusti, R., 2019. Development and validation of a multianalyte method for quantification of mycotoxins and pesticides in rice using a simple dilute and shoot procedure and UHPLC-MS/MS. Food Chem. 270, 420–427. https://doi.org/10.1016/j.foodchem.2018.07.126.
Sun, J., Wu, Y., 2016. Evaluation of dietary exposure to deoxynivalenol (DON) and its derivatives from cereals in China. Food Contr. 69, 90–99. https://doi.org/10.1016/j.foodcont.2016.04.040.
Taghizadeh, S.F., Rezaee, R., Badiebostan, H., Giesy, J.P., Gholamreza Karimi, G., 2020. Occurrence of mycotoxins in rice consumed by Iranians: a probabilistic assessment of

risk to health. Food Addit. Contam. 37 (2), 342–354. https://doi.org/10.1080/19440049.2019.1684572.

Taniwaki, M.H., Pitt, J.I., Copetti, M.V., Teixeira, A.A., Iamanaka, B.T., 2019. Understanding mycotoxin contamination across the food chain in Brazil: challenges and opportunities. Toxins 11 (411), 1–17. https://doi.org/10.3390/toxins11070411.

Tennant, D., Bánáti, D., Kennedy, M., König, J., O'Mahony, C., Kettler, S., 2017. Assessing and reporting uncertainties in dietary exposure analysis - Part II: application of the uncertainty template to a practical example of exposure assessment. Food Chem. Toxicol. 109 (Pt 1), 68–80. https://doi.org/10.1016/j.fct.2017.07.061.

Tralamazza, S.M., Bemvenuti, R.H., Zorzete, P., De Souza Garcia, F., Corrêa, B., 2016. Fungal diversity and natural occurrence of deoxynivalenol and zearalenone in freshly harvested wheat grains from Brazil. Food Chem. 1 (196), 445–450. https://doi.org/10.1016/j.foodchem.2015.09.063.

Ueno, Y., Iijima, K., Wang, S.-D., Sugiura, Y., Sekijima, M., Tanaka, T., Chen, C., Yu, S.-Z., 1997. Fumonisins as a possible contributory risk factor for primary liver cancer: a 3-year study of corn harvested in Haimen, China, by HPLC and ELISA. Food Chem. Toxicol. 35, 1143–1150. https://doi.org/10.1016/S0278-6915(97)00113-0.

Van der Voet, H., Kruisselbrink, J., Boer, W.J. de, Boon, P.E., 2014. Model-Then-Add Usual intake modelling of multimodal intake distributions. RIVM Letter report 090133001/2014. accessed 19 April 2020. https://rivm.openrepository.com/bitstream/handle/10029/314361/090133001.pdf?sequence=3, 24.

Van de Walle, J., During, A., Piront, N., Toussaint, O., Schneider, Y.J., Larondelle, Y., 2010. Physio-pathological parameters affect the activation of inflammatory pathways by deoxynivalenol in Caco-2 cells. Toxicol. Vitro 24 (7), 1890–1898. https://doi.org/10.1016/j.tiv.2010.07.008.

Waes, J.G., Starr, L., Maddox, J., Aleman, F., Voss, K.A., Wilberding, J., Riley, R.T., 2005. Maternal fumonisin exposure and risk for neural tube Defects : mechanisms in an in vivo mouse model. Adv. Food Nutr. Res. 497, 487–497. https://doi.org/10.1002/bdra.20148.

WHO. World Health Organization & International Programme on Chemical Safety, 2018. Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization, second ed. World Health Organization https://apps.who.int/iris/handle/10665/259858. License: CC BY-NC-SA 3.0 IGO.

Xue, K.S., Tang, L., Sun, G., Wang, S., Hu, X., Wang, J.S., 2019. Mycotoxin exposure is associated with increased risk of esophageal squamous cell carcinoma in Huaian area, China. BMC Canc. 19 (1), 1218. https://doi.org/10.1186/s12885-019-6439-x.