

Multi-Mycotoxins in Corn Products, Crackers, Other Grain Products, Pasta and Gluten-Free Products - April 1, 2018 to March 31, 2019

Food chemistry - Targeted surveys - Final report

Summary

Targeted surveys provide information on potential food hazards and enhance the Canadian Food Inspection Agency's (CFIA's) routine monitoring programs. These surveys provide evidence regarding the safety of the food supply, identify potential emerging hazards, and contribute new information and data to food categories where it may be limited or non-existent. They are often used by the Agency to focus surveillance on potential areas of higher risk. Surveys can also help to identify trends and provide information about how industry complies with Canadian regulations.

The main objectives of this targeted survey were to expand baseline data on the presence and levels of mycotoxins in corn products, crackers, other grain (non-staple) products, pasta and gluten-free products; and to compare these results to other data, where feasible. Mycotoxins are natural toxins released by moulds that infect agricultural crops before and after harvest. Their human health effects are varied; the health effects depend on the type and level of mycotoxin in the food. Canada does not have maximum levels for the mycotoxins in the products targeted in this survey, with the exception of ochratoxin A (OTA), for which Canada has proposed maximum levels in certain foods.

A total of 750 samples corn and pasta products, crackers, gluten-free and other grain products were analyzed for the presence of mycotoxins. Mycotoxins were detected in 388 samples (52%). A total of 17 different mycotoxins were detected in the product types sampled by this survey. Aflatoxin G2, 3-acetyldeoxynivalenol (3-Ac-DON), 15-acetyldeoxynivalenol (15-Ac-DON), neosolaniol (NEO), diacetoxyscirpenol (DAS), fusarenone-X (FUS-X), alpha-zeranol, and beta-zeranol were not detected in any of the samples. The mycotoxin detected most frequently was deoxynivalenol (DON) in a total of 306 samples (41%).

All mycotoxin results were assessed by Health Canada's Bureau of Chemical Safety (BCS). Health Canada's BCS concluded that the levels detected in this survey were not expected to pose a human health concern. No product recalls were warranted given the lack of a human health concern.

What are targeted surveys

Targeted surveys are used by the CFIA to focus its surveillance activities on areas of highest health risk. The information gained from these surveys provides support for the allocation and prioritization of the Agency's activities to areas of greater concern. Originally started as a project under the Food Safety Action Plan (FSAP), targeted surveys have been embedded in our regular surveillance activities since 2013. Targeted surveys are a valuable tool for generating information on certain hazards in foods, identifying and characterizing new and emerging hazards, informing trend analysis, prompting and refining health risk assessments, highlighting potential contamination issues, as well as assessing and promoting compliance with Canadian regulations.

Food safety is a shared responsibility. We work with federal, provincial, territorial and municipal governments and provide regulatory oversight of the food industry to promote safe handling of foods throughout the food production chain. The food industry and retail sectors in Canada are responsible for the food they produce and sell, while individual consumers are responsible for the safe handling of the food they have in their possession.

Why did we conduct this survey

Mycotoxins are natural toxins released by moulds that can grow on crops in the field or after harvest¹. These toxins are released by moulds which can grow on agricultural products, such as on cereals (e.g. wheat, oats, and corn), legumes, nuts and fruit. The type of agricultural product, insect damage, and the climatic conditions (temperature, humidity) during growth, processing, and storage are some factors that can influence the types and levels of mycotoxins present in the foods available at the retail level². The human health effects are varied; ranging from gastrointestinal distress to cancer, the health effects depend on the type and level of mycotoxin in the food.

Research has shown that of the hundreds of mycotoxins associated with food, a small fraction has the potential to adversely affect human health and pose a global health concern². The Codex Alimentarius Commission is an international body established by the United Nations' Food and Agriculture Organization and the World Health Organization to develop harmonized international food standards, guidelines, and codes of practice to protect the health of the consumers and to ensure fair practices in the food trade. Codex has published a Code of Practice to reduce and prevent mycotoxin contamination in cereals (e.g., wheat, corn, oats, and barley)². This Code of Practice acknowledges that the complete elimination of mycotoxins from foods is not possible but

it provides guidance on ways to control and manage the mycotoxin levels at the farm level and after harvest (for example, during processing, storage, and transport).

There are now more than 300 known mycotoxins of widely different chemical structures and differing modes of action - some target the kidney, liver, or immune system and some are carcinogenic. Common mycotoxins include aflatoxins, ochratoxin A, ergot alkaloids, fumonisins, trichothecenes (such as deoxynivalenol which is also known as vomitoxin) and zearalenone^{Error!}

Please see <u>Appendix A</u> for a description of the different mycotoxins included in this study and their health effects.

What did we sample

A variety of domestic and imported corn products, crackers, other grain (non-staple) products, pasta and gluten-free products were sampled between April 1, 2018 and March 31, 2019. Samples of products were collected from local/regional retail locations located in 6 major cities across Canada. These cities encompassed 4 Canadian geographical areas: Atlantic (Halifax), Quebec (Montreal), Ontario (Toronto, Ottawa) and the West (Vancouver, and Calgary). The number of samples collected from these cities was in proportion to the relative population of the respective areas. The shelf life, storage conditions, and the cost of the food on the open market were not considered in this survey.

Product type	Number of domestic samples	Number of imported ^a samples	Number of samples of unspecified ^b origin	Total number of samples
Corn products	12	80	44	136
Crackers	7	41	54	102
Gluten-free products	17	35	18	70
Other grains	73	76	148	297
Pasta	46	73	26	145
Grand total	155	305	290	750

Table 1. Distribution of samples based on product type and origin

^a Imported from at least 27 countries

^b Unspecified refers to those samples for which the country of origin could not be assigned from the product label or available sample information

How were samples analyzed and assessed

Samples were analyzed by an ISO/IEC 17025 accredited food testing laboratory under contract with the Government of Canada. See Appendix A for a list of the pesticides analyzed. The results are based on the food products as sold and not necessarily as they would be consumed.

Health Canada has not established tolerances or standards for the majority of the mycotoxins in the grain products targeted in this survey. In 2009, Health Canada proposed maximum levels (ML) for OTA in a variety of foods. An ML of 3 ppb has been proposed for grains for direct consumption and derived cereal products (for example flour, bread, breakfast cereal), an ML of 7 ppb has been proposed for wheat bran and an ML of 0.5 ppb has been proposed for infant formulas and cereal-based foods³. These MLs as well as an industry guidance value for OTA in unprocessed cereal grains are still under consideration.

In the absence of applicable tolerances or standards, high levels of mycotoxins may be assessed by Health Canada's Bureau of Chemical Safety (BCS) on a case-by-case basis using the most current scientific data available.

What were the survey results

Multi-mycotoxins

A total of 750 samples were analyzed for the presence of mycotoxins. The products sampled were separated into 5 product types: corn products, crackers, other grain products, pasta, and gluten-free products. Mycotoxins were detected in 388 samples (52%). A total of 17 different mycotoxins were detected in the product types sampled by this survey. Aflatoxin G2, 3-Ac-DON, 15-Ac-DON, NEO, DAS, FUS-X, alpha-zeranol, and beta-zeranol were not detected in any of the samples. Table 2 illustrates the number of samples with detectable levels of mycotoxins for all of the product types. Pasta and gluten-free products have the highest and lowest percentage of detectable mycotoxins, respectively.

Product type	Number of samples	Number (percentage) of samples with detected mycotoxin(s)	Number (percentage) of samples with no detected mycotoxin(s)	Number of mycotoxins per sample
Corn products	136	92 (68%)	44 (32%)	1-9
Crackers	102	70 (69%)	32 (31%)	1-2
Gluten-free products	70	17 (24%)	53 (76%)	1-4
Other grains	297	103 (35%)	194 (65%)	1-4
Pasta	145	104 (72%)	41 (28%)	1-5
Grand total	750	386 (51%)	364 (49%)	1-9

Table 2. Results of multi-m	vcotoxin testing in	grain-based products
	ycoloxin leading in	gram-based products

As can be seen from Table 2, up to 9 mycotoxins were detected per sample. These may consist of mycotoxin families (3 forms of aflatoxin or 3 forms of fumonisin) or discrete mycotoxins (for example, sterigmatocystin). The mycotoxin detected most frequently was deoxynivalenol in a total of 306 samples (41%). The least commonly detected mycotoxin was aflatoxin B2; detected in only one sample. The levels of mycotoxins ranged from 0.4 ppb to 2570 ppb.

What do the survey results mean

In comparison to previous survey years^{4,5,6,7} the detection rates for mycotoxins in various types of grain-based foods were consistent, with the exception of cyclopiazonic acid and zearalenone and its derivatives (Table 3). This may be related to differences in product types, conditions during a specific cultivation year, and source of the grains. Health Canada has not set or proposed limits for any of the mycotoxins for these surveys, with the exception of OTA. The compliance rate for grain based products for OTA (99.1%) was comparable to previous survey years (97.3% to 99.6%). As observed in previous surveys, DON was the most commonly observed mycotoxin. HC determined the levels of mycotoxins in the grain-based foods observed in the current survey are not expected to pose a concern to human health, therefore there were no recalls resulting from this survey.

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Survey author	Year	Analyte	Number of samples	Number of samples with detectable mycotoxins (percentage)	Maximu m mycotoxi n level (ppb)	Average* mycotoxi n level (ppb)
CFIA	2018	Aflatoxins B1, B2, and G1	750	11 (1.5)	30	4.4
CFIA	2017	Aflatoxins B1, B2, and G1	748	4 (0.5)	4.6	4.3
CFIA	2016	Aflatoxins B1, B2, and G1	751	4 (0.5)	7.6	5.0
CFIA	2015	Aflatoxins B1, B2, and G1	745	6 (0.8)	1.4	0.9
CFIA	2013 to 2015	Aflatoxins B1, B2, and G1	2235	57 (2.5)	17	3.6
CFIA	2015 to 2019	3- and 15- acetyldeoxynivale nol (2994	0 (0)	-	-
CFIA	2013 to 2015	3- and 15- acetyldeoxynivale nol	2235	8 (0.004)	53	35.25
CFIA	2018	Deoxynivalenol	750	306 (41)	2570	282
CFIA	2017	Deoxynivalenol	748	440 (59)	1000	160
CFIA	2016	Deoxynivalenol	751	245 (33)	1360	176
CFIA	2015	Deoxynivalenol	745	203 (27)	3900	232
CFIA	2013 to 2015	Deoxynivalenol	2235	1044 (46)	2330	176
CFIA	2018	Diacetoxyscirpen ol	750	0 (0)	-	-
CFIA	2017	Diacetoxyscirpenol	748	0 (0)	-	-
CFIA	2016	Diacetoxyscirpenol	751	1 (0.1)	10	10
CFIA	2015	Diacetoxyscirpenol	745	4 (0.5)	250	115
CFIA	2013 to 2015	Diacetoxyscirpenol	2235	0 (0.0)	-	-
		Fusarenone-X	750	0 (0)	-	-
CFIA	2017	Fusarenone-X	748	0 (0)	-	-
CFIA	2016	Fusarenone-X	751	1 (0.1)	23	23
CFIA	2015	Fusarenone-X	745	0 (0)	-	-
CFIA	2013 to 2015	Fusarenone-X	2235	0 (0.0)	-	-
		Neosolaniol	750	0 (0.0)	-	-
CFIA	2017	Neosolaniol	748	1 (0.1)	20	20
CFIA	2016	Neosolaniol	751	0 (0)	-	-
CFIA	2015	Neosolaniol	745	0 (0)	-	-

 Table 3. Mycotoxin testing results in grain-based products from various survey years

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Survey author	Year	Analyte	Number of samples	Number of samples with detectable mycotoxins (percentage)	Maximu m mycotoxi n level (ppb)	Average* mycotoxi n level (ppb)
CFIA	2013 to 2015	Neosolaniol	2235	1 (0.0004)	30	30
CFIA	2018	Nivalenol	750	7 (0.9)	86	22
CFIA	2017	Nivalenol	748	6 (0.8)	47	28
CFIA	2016	Nivalenol	751	0 (0)	-	-
CFIA	2015	Nivalenol	745	1 (0.1)	17	17
CFIA	2013 to 2015	Nivalenol	2235	4 (0.002)	98	42
CFIA	2018	Ergot Alkaloids	750	46 (6.1)	664	79
CFIA	2017	Ergot Alkaloids	748	231 (31)	1060	60
CFIA	2016	Ergot Alkaloids	751	63 (8.4)	1530	138
CFIA	2015	Ergot Alkaloids	745	85 (11)	1145	110
CFIA	2013 to 2015	Ergot Alkaloids	2235	478 (21.4)	1078	62
CFIA	2018	Fumonisins B ₁ , B ₂ and B ₃	750	105 (14)	3503	280
CFIA	2017	Fumonisins B_1 , B_2 and B_3	748	21 (2.8)	864	90
CFIA	2016	Fumonisins B_1 , B_2 and B_3	751	48 (6.4)	2209	430
CFIA	2015	Fumonisins B_1 , B_2 and B_3	745	30 (4.0)	1142	214
CFIA	2013 to 2015	Fumonisins B ₁ , B ₂ and B ₃	2235	233 (10)	2062	187
CFIA	2011	Fumonisins B_1 and B_2	274	161 (59)	4442	253
CFIA	2018	HT-2 and T-2 toxin	750	8 (1.1)	98	37
CFIA	2017	HT-2 and T-2 toxin	748	8 (1.1)	98	15
CFIA	2016	HT-2 and T-2 toxin	751	19 (2.5)	85	21
CFIA	2015	HT-2 and T-2 toxin	745	11 (1.5)	32	17
CFIA	2013 to 2015	HT-2 and T-2 toxin	2235	66 (2.9)	271	28
CFIA	2018	Cyclopiazonic acid	750	18 (2.4)	47	11
CFIA	2017	Cyclopiazonic acid	748	4 (0.5)	6.5	2.5
CFIA	2016	Cyclopiazonic acid	751	1 (0.1)	2.5	2.5
CFIA	2015	Cyclopiazonic acid	745	5 (0.7)	3.1	1.9
CFIA	2013 to 2015	Cyclopiazonic acid	2235	35 (1.5)	8.3	2.7
CFIA	2018	Ochratoxin A	750	20 (2.7)	34	4.2
CFIA	2017	Ochratoxin A	748	35 (4.7)	267	10
CFIA	2016	Ochratoxin A	751	20 (2.7)	20	2.7

Survey author	Year	Analyte	Number of samples	Number of samples with detectable mycotoxins (percentage)	Maximu m mycotoxi n level (ppb)	Average* mycotoxi n level (ppb)
CFIA	2015	Ochratoxin A	745	36 (4.8)	36	4.8
CFIA	2013	Ochratoxin A	2235	128 (5.7)	34	2.6
	to 2015					
CFIA	2018	Sterigmatocystin	750	12 (1.6)	12	2.7
CFIA	2017	Sterigmatocystin	748	26 (3.5)	12	2.8
CFIA	2016	Sterigmatocystin	751	40 (5.3)	34	3.0
CFIA	2015	Sterigmatocystin	745	32 (4.3)	28	5.7
CFIA	2013 to 2015	Sterigmatocystin	2235	41 (1.8)	18	3.1
CFIA	2018	Zearalenone, α- zearalenol and β- zearalenol	750	34 (4.5)	450	44
CFIA	2017	Zearalenone, α- zearalenol and β- zearalenol	748	12 (1.6)	199	46
CFIA	2016	Zearalenone, α- zearalenol and β- zearalenol	751	23 (3.1)	145	39
CFIA	2015	Zearalenone, α- zearalenol and β- zearalenol	745	23 (3.1)	477	88
CFIA	2013 to 2015	Zearalenone, α- zearalenol and β- zearalenol	2235	93 (4.0)	577	50

*Average of positive results only

Appendix A

1 Aflatoxins

Aflatoxins are a family of naturally-occurring, toxic secondary metabolites produced by *Aspergillus flavus* and *A. parasiticus* fungi⁸. Aflatoxin-producing fungi may contaminate agricultural products (such as corn, nuts, spices, dried fruit) if grown, transported, stored, or processed under hot, humid conditions for prolonged periods of time, or with pest pressures resulting in bruising or cuts on the commodity^{8,9}. Drought pressure on corn is also a major risk factor for the occurrence of aflatoxins in the field^{8,9,10}. Due to the cooler Canadian climate, domestically-grown agricultural commodities (and products) are less likely to contain aflatoxins than those imported from warmer climates. Aflatoxins are not destroyed by heating, cooking or most other processing methods¹¹.

One aflatoxin form, aflatoxin B1, is among the most potent naturally-occurring liver carcinogens known¹². The International Agency for Research on Cancer (IARC) classified aflatoxins to be carcinogenic to humans (Group 1 carcinogen)¹³. Chronic exposure to aflatoxins has also been associated with growth impairment in children living in developing countries where exposure to aflatoxins is relatively high. Aflatoxins have been shown to cause immune suppression in experimental animals^{14,15,16,17}. Short-term exposure to high levels of aflatoxins can cause illness in humans which is characterized by vomiting, abdominal pain, convulsions, coma and death. The illness is very rare in the developed world¹⁸. This study included aflatoxins B1, B2, G1 and G2.

2 Cyclopiazonic Acid

Cyclopiazonic acid (CPA) is produced by *Penicillium cyclopium, Penicillium* species (e.g. *P. commune* and *P. camembertii*), *Aspergillus flavus and A. versicolor*. Cyclopiazonic acid has been detected in corn, millet, peanuts, pulses, cheese, ham, sausage, hot dogs, tomato and milk¹⁹.

There is little information available regarding potential human health effects associated with CPA. However, it has been linked to 'Kodua' poisoning in India resulting from ingestion of contaminated millet seeds. The symptoms included sleepiness, tremors and giddiness which lasted 1-3 days, followed by complete recovery²⁰. Experimental animal studies indicate that CPA is toxic only when ingested in high concentrations. Repeat exposure to high doses of CPA show a range of effects such as neurotoxicity, liver and kidney damage, weight loss, diarrhea, dehydration, convulsions and death in several different species²¹.

3 Ergot Alkaloids

Ergot alkaloids are formed by fungi of the *Claviceps* species, particularly *C. purpurea*. These fungi parasitize the seed heads of cereals, replacing individual grain kernels with discoloured fungal structures (dark purple or black) known as sclerotia or ergot bodies. The predominant ergot

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alkaloids present in ergot bodies are ergometrine, ergotamine, ergosine, ergocristine, ergocryptine and ergocornine (only ergosine, ergocristine and ergocryptine were successfully included in the current multi-mycotoxin method). The type and levels of these alkaloids in ergot bodies vary considerably depending on the fungal strain, the host species, the weather conditions and geographic region. Wet weather and soil favour the growth of ergot bodies. These bodies are harvested with the cereals and can thus lead to contamination of cereal based food and feed products with ergot alkaloids. The cleaning methods used during grain processing usually remove the ergot bodies from the grain²².

Long-term exposure to ergot alkaloids causes ergotism, also known as ergotoxicosis, ergot poisoning and Saint Anthony's Fire^{23,24}. The symptoms can include fevers, hallucinations, swollen or rigid limbs, severe inflammation sometimes followed by loss of affected tissues and death²⁵. Experimental animal studies indicate the ergot alkaloids act on a number of neurotransmitter receptors which with repeat dosing results in restricted blood flow, particularly of the limbs, weight loss and changes in the levels of some hormones in rats²⁶. This study included ergosine, ergocristine and ergocryptine.

4 Fumonisins

Fusarium moniliforme and *Fusarium proliferatum* are plant pathogens common in grain-growing regions throughout the world. These pathogens can infect grain crops either in the field (pre-harvest) or during storage (post-harvest). The moulds proliferate if grains are grown in hot, dry weather followed by very humid conditions. Mould growth is also favoured by storage under wet conditions. The plant pathogens produce mycotoxins known as fumonisins. Corn is the grain most vulnerable to fumonisin contamination²⁷. The levels of fumonisins can be quite high, even in the absence of visible signs of mould proliferation²⁸. There are several forms of fumonisin: fumonisins B1, B2 and B3 are the most prevalent. While studies have focused on fumonisin B1, available data suggests that fumonisins B2 and B3 have a similar toxicological profile^{29,30,31,32}. Fumonisins are heat-stable up to 150°C and are unaffected by mechanical forces (such as grinding), but can be reduced by alkaline treatment (a traditional means of preparing corn masa and other cornbased products such as tacos)³³.

Although fumonisin contamination is mainly observed in corn, some scientific studies have shown the presence of fumonisins in red wine³⁴, sorghum³⁵, white beans, wheat^{Error! Bookmark not defined.}, barley^{Error! Bookmark not defined.}, soybeans^{Error! Bookmark not defined.}, figs^{Error! Bookmark not defined.}, rice³⁶, black tea^{Error! Bookmark not defined.}, and medicinal herbs^{Error! Bookmark not defined.}

The ingestion of foods containing fumonisins may be harmful to human health. Health effects which have been observed in specific populations where corn is a major component of the diet and where the climate may favor fumonisin proliferation include esophageal cancer in South

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Africa and China^{Error! Bookmark not defined.,37}, neural tube defects in Central America and the southwestern US³². The precise biological effects of fumonisins are complex and relate to their interference with cell metabolism^{Error! Bookmark not defined.}. Experimental animal studies have revealed that fumonisins induce liver and kidney damage in many species³⁸. Fumonisin B1 has been classified by IARC as possibly carcinogenic to humans based on evidence in experimental animal studies³⁹. This study included fumonisins B1, B2 and B3.

5 Ochratoxin A (OTA)

OTA is a naturally occurring metabolite of *Aspergillus* and *Penicillium* moulds. Under favourable moisture and temperature conditions, the fungi can grow on stored material and produce OTA⁴⁰. OTA has been widely detected in cereal grains (wheat, corn, oat, and barley), green coffee, grape juice, beer, wines, cocoa, dried fruits, and nuts⁴¹. OTA is heat-stable and is only partially destroyed under normal cooking or processing conditions⁴².

The International Agency for Research on Cancer (IARC) has classified OTA as a possible human carcinogen based largely on data from animal studies⁴³. The mechanism by which OTA causes kidney tumours in rodents has yet to be fully explained. In animal studies, OTA has also been shown to have effects on the kidneys, the developing fetus, and the immune system. Health Canada completed a risk assessment for OTA, and as a result, has proposed maximum levels for OTA in various food commodities^{Error! Bookmark not defined.} as well as an industry guidance value for OTA in unprocessed cereal grains^{Error! Bookmark not defined.}

6 Sterigmatocystin

Sterigmatocystin is a mycotoxin produced mainly by various *Aspergillus* species. It can also be produced by species such *as Bipolaris, Chaetomium*, and *Emiricella*. It has been detected in grains, corn, bread, cheese, spices, coffee beans, soybeans, and pistachio nuts. Wet, warm, conditions favour sterigmatocystin production⁴⁴.

The IARC has classified sterigmatocystin as a possible human carcinogen⁴⁵. It also has properties capable of causing DNA mutations. It is acutely toxic to animals, with the liver and kidneys as its principle targets. This toxin is structurally similar to aflatoxin, however, tests in rats have shown that it is ten times less lethal following acute exposure to high doses and ten to a hundred times less effective at inducing liver cancer^{Error! Bookmark not defined.} Its human health effects have not been well-studied.

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7 Trichothecenes

This large family of mycotoxins are typically found in cereal grains (notably wheat, barley, and corn), and have been detected in their derived products (flours, meals, bran, grits, cereals, and beer). These toxins are produced by various species of *Fusarium* mould in some crops prior to harvest. These toxins are observed in grains suffering from Fusarium head blight (FHB) in the field. Wet, warm weather conditions in the field will favour the development of FHB, and subsequently the production of trichothecenes⁴⁶. The trichothecenes are heat-stable and are only partially destroyed under normal cooking or processing conditions⁴⁷. The most widely commonly occurring trichothenece is DON.

The human health effects of nivalenol⁴⁸, fusarenone⁴⁹, 3-Ac-DON^{Error! Bookmark not defined.}, 15-Ac-DON^{Error! Bookmark not defined.6}, neosolaniol NEO^{Error! Bookmark not defined.6} and DAS^{Error! Bookmark not defined.6} are not as well-studied as those of DON. DON is not known to be carcinogenic, but it has been associated with acute and chronic health effects. Outbreaks in Asia, attributed to the consumption of grains with high levels of DON, are associated with short-term human illness, involving nausea, vomiting, abdominal pain, headache and dizziness. In experimental animal studies, long-term exposures to low levels of DON are associated with decreased food intake, weight loss, and effects on the immune system⁵⁰.

T-2 and HT-2 toxins are formed when grain crops remain in the field at or after harvest for extended periods, especially in cold weather, or in grain that becomes wet during storage. They have been detected in wheat, corn, oats, barley, rice, beans, and soybeans and some cereal-based products. Oats are most likely to contain these toxins but they have been detected frequently at lower concentrations in barley. Wheat is only rarely contaminated with these toxins⁵¹.

The human health effects associated with chronic exposure to HT-2 and T-2 are not known. In animals, these toxins inhibit DNA, RNA and protein synthesis and are cytotoxic. IARC considers HT-2/T-2 toxins not classifiable as to their carcinogenicity to humans based on the lack of available human carcinogenicity data and only limited evidence in experimental animals^{52,53}. This study examined nivalenol, fusarenone, 3-Ac-DON, 15-Ac-DON, NEO, DAS, DON, HT-2 and T-2.

8 Zearalenone and Related Compounds

Zearalenone (ZEN) is a mycotoxin produced mainly by *Fusarium* species. It has been detected in wheat, barley, rice, corn, and other cereals. It is heat-resistant and can be found in finished grain-based products. ZEN is metabolised to α -zearalenol (α -ZOL) and β -zearalenol (β -ZOL)^{54,55,56}.

ZEN is not an acute toxin. ZEN is an estrogenic compound and its major metabolites are more potent estrogenic compounds. It causes infertility in sheep, cattle and pigs, and may lead to earlier sexual maturation in some animals. In experimental animal studies, high oral doses of ZEN have also been shown to be genotoxic, toxic to the liver, and affect blood and the immune system^{Error! Bookmark not defined.3,57}. IARC concluded that there is limited evidence of the carcinogenicity of ZEN⁵⁸. ZEN has been considered a possible contributing agent in the outbreaks of early puberty in thousands of girls in Puerto Rico and may play a role in human breast and cervical cancer in highly exposed populations^{Error! Bookmark not defined.}

This study examined ZEN α -ZOL, and β -ZOL.

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