MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evalution

Risk Assessment of Mycotoxins

Mycotoxins are secondary metabolites produced by fungi that cause disease or abnormal physiological activity in humans and cattle, and are often found in grains, nuts, and plants, that; are conducive to fungal growth. Many mycotoxins commonly found in plants are known to be produced by fungi from a few select genera: *Aspergillus* (producing aflatoxins, cyclopiazonic acid, ochratoxin, and sterigmatocystin), *Penicillium* (producing ochratoxin and patulin), and *Fusarium* (producing deoxynivalenol, T-2 toxin, fumonisin, and zearalenone).

South Korea began controlling mycotoxins in 1999, setting temporary acceptable limits for both aflatoxin B1 (in grains, pulses, and nuts) and aflatoxin M1 (in raw milk and milk products before processing). Since then, limits have been established for total aflatoxins (sum of B_1, B_2, G_1, and G_2), aflatoxin M_1, fumonisin, ochratoxin, deoxynivalenol, and zearalenone in relevant foods based on international food standards (CODEX Alimentarius Commission) and regulations in other countries.

The CODEX specifies limits for total aflatoxins in nuts, ochratoxin A, and deoxynivalenol in grains, patulin in apple juice and apple juice ingredients in other beverages, and deoxynivalenol in for infants and toddler foods. For other mycotoxins, the “Code of Practice for the Prevention and Reduction of Mycotoxin Contamination in Cereals (CAC/RCP 51-2003)” was prepared, and studies are underway to establish maximum levels for other categories, such as spices and ergot alkaloids.

Mycotoxins are a relatively new safety consideration for foodstuffs because of an increase in the long-term storage and transportation that accompanies mass production and international trade. Moreover, climate change severely affects not only land use, crop production, and soil quality, but also manufacture, transport, and storage conditions for crops and plants.

Particularly, changes in climatic factors such as air temperature, relative humidity, and precipitation impact the growth of *Aspergillus*, *Penicillium*, and *Fusarium* spp., which typically inhabit crops and plants, as well as produce mycotoxins such as aflatoxin, ochratoxin, deoxynivalenol, and fumonisin. This may lead to severe negative consequences for the health of humans and other animals.

As a result, the safety management of mycotoxins in plants is very important, and the Korean Ministry of Food and Drug Safety has enacted large-scale monitoring projects and risk assessments for foods in domestic circulation.

Mycotoxins are metabolites produced by fungi that are present at varying levels in grains and processed foods. Their prevalence can increase following fungi infection during the cultivation of plants used for food, particularly when weather conditions are favourable or parasitic infections. They can also be produced during storage and circulation, either industrially or at home. Tables 1 and 2 display general and toxicity information for major mycotoxins.

Table 1. General information of major mycotoxins

Mycotoxin	Main source of contamination	Fungus name	Susceptible groups	Symptoms	Susceptible areas	Stressors
Aflatoxin	Corn, rice, peanuts, sorghum, cotton	*A. flavus* *A. parasiticus*	Dairy, cows, Pigs, Poultry	Loss of appetite, Reduced milk yield, Impaired immunity, Liver cancer	Warm, dry regions	Drought Heat wave

Deoxynivalenol	Corn, wheat, bran, rice, wheat flour, malt, barley	*Fusarium graminearum*	Cattle, Pigs, Sheep	Vomiting , Food refusal, Diarrhea, Weight loss, Reduced milk yield	Humid regions that are cold at night and warm during the day	Flood, High humidity, Large temperature changes
Zearalenone	Corn, wheat, bran, rice, malt, barley	*Fusarium graminearum*	Pigs, Poultry	Vaginitis, Premature birth, Miscarriage, Anal swelling	Humid regions that are cold at night and warm during the day	Flood, High humidity, Large temperature changes
Ochratoxin	Coffee, grains	*A. ochraceous Penicillium spp.*	Pigs, Poultry	Impaired growth, Loss of appetite, Food refusal, Renal disease, Renal impairment, Death	Warm regions	Drought, Heat wave
Fumonisin	Corn	*F. moniliforme F. proliferatum*	Horses, Pigs	Blindness, Head-butting, Loss of balance, Pulmonary edema, Hepatopancreatic disorders, Esophageal cancer	Warm regions	Drought, High humidity

Table 2. Toxicity information of major mycotoxins

Mycotoxin	Units	TDI	TDI***	IARC
Aflatoxin B1	Not established		$BMDL_{10}$ = 170 ng/kg bw/day	GROUP 1
Aflatoxin M1				GROUP 2B
Ochratoxin A	PTWI*	1.0	0.11 μg/kg bw/week	GROUP 2B
Fumonisin	TDI**	2.0	1.65 μg/kg bw/day	GROUP 2B
Patulin		0.4	0.4 μg/kg bw/day	GROUP 3
Deoxynivalenol		1.0	1 μg/kg bw /day	GROUP 3
Zearalenone		0.5	0.4 μg/kg bw /day	GROUP 3

* PTWI: Provisional tolerable weekly intake (ng/kg bw/week)

** TDI: Tolerable daily intake (ng/kg bw/day)

*** As designated by the National Institute of Food and Drug Safety Evaluation

For the risk assessment evaluation, an exposure assessment was conducted in accordance with Article 4, Clause 3 of the "Enforcement Decree of the Food Sanitation Act (Presidential Decree No. 27398, 26. Jul, 2016, Partial Amendment)" and the CODEX "Statement of Principle Relating to the Role of Food Safety Risk Assessment". The report was compiled according to the four stages of risk assessment: hazard identification, hazard characterization, exposure assessment, and risk characterization, as specified by the "Risk Assessment Report Compilation Guidelines (July 2015, Ministry of Food and Drug Safety)".

This report aimed to investigate the level of mycotoxin contamination in domestically circulating food products for eight mycotoxins, based on the standards and regulations in the CODEX (total aflatoxin [aflatoxin B_1], aflatoxin M_1, deoxynivalenol, ochratoxin A, zearalenone, fumonisin, and patulin). The goals were to calculate potential human mycotoxin exposure based on typical food intake in the Korean population. Particularly, unlike previous

risk assessments that focused on individual food products, this study evaluated food groups (agricultural products) with the highest risk of mycotoxin exposure among those consumed regularly by the Korean population, making the results more representative.

The contamination data used in this study included the test results of Public Health and Environment Research Institutes from 16 cities, as part of the 2012–2014 "Comprehensive Plan for the Safety Control of Hazardous Substances" and the 2015 "Project to Reassess Standards and Regulations for Unintended Hazardous Substances". In total, 45,383 samples were analyzed across 473 categories of domestic circulating food products. Between 2012 and 2014, food products analyzed to verify mycotoxin contamination levels were selected based on food groups with established standards. In 2015, high-consumption, high-frequency foods were selected based on daily intake surveys as part of the Korea National Health and Nutrition Examination Survey (KNHANES, 2011–13). Seafood was excluded from the analysis because of the low likelihood of mycotoxin contamination. The food products designated by the Public Health and Environment Research Institutes in 16 cities were purchased from supermarkets and markets in those regions. There were 10,443 samples from 300 products for aflatoxin, 473 samples from 17 products for aflatoxin M_1, 9,586 samples from 298 products for ochratoxin A, 4,338 samples from 211 products for deoxynivalenol, 4,614 samples from 214 products for zearalenone, 5,165 samples from 2,215 products for fumonisin, and 321 samples from 12 products for patulin .

Samples were analyzed using high-performance liquid chromatography (HPLC) and mass spectrometry (MS), according to the CODEX HPLC or HPLC/MS/MS method, while "non-detects" were evaluated using ND (0) and ND (limit of detection, LOD). "Detect" samples were included in all exposure assessments, regardless of the number of samples; when the number of samples was less than 10, ND samples were excluded from the exposure assessment for reasons related to statistical significance.

Although the level of detection in the surveyed food products was very low, to account for the intake level in the Korean population when evaluating potential exposure levels, non-detection was classified as ND (0) or ND (LOD).

Daily mycotoxin exposure (μg/kg bw/day) for the study population was calculated using the following formula:

$$\frac{\text{Mycotoxin contamination of the food (mg/kg)} \times \text{food intake of the population (g/day)}}{\text{Mean body weight of the population (kg)}}$$

The mycotoxin risk from food intake was assessed by the margin of exposure (MOE) method for aflatoxin, while the risk (%) for five types of mycotoxin, including ochratoxin A, was assessed using health-based guidance values (HBGVs).

$$\text{MOE} = \frac{\text{No-observed-adverse-effect level (μg/kg bw/day)}}{\text{Daily exposure (μg/kg bw/day)}}$$

$$\text{Risk (\%)} = \frac{\text{Daily exposure (μg/kg bw/day)}}{\text{HBGV (tolerable daily intake (μg/kg bw/day))}} \times 100$$

For food intake used to calculate exposure, the mean and extreme intake (P95) levels were taken, by age, from the 2011–13 KNHANES, and rounded to three decimal places.

The mean body weight of subjects in KNHANES V (Years 2–3, 2011–2012) and VI (Year 1, 2013) were calculated using the MIMS/MAP 3.0 & Oracle 10g programs. Table 4 displays the mean body weight by age.

Table 4. Mean body weight (kg), by age

All	≤2 years	3–6 years	7–12 years	13–19 years	20–64 years	≥65 years	Adults (≥20 years)
59.33	12.23	19.08	37.24	59.69	65.11	58.40	64.09

Of the eight mycotoxins tested, deoxynivalenol (DON), ochratoxin A (OTA), zearalenone (ZEA), fumonisin (FUM), and patulin (PAT) showed very low detection rates in foods and very low levels of contamination. Among these five mycotoxins, the maximum detection rate in food was 7.7%, which is very low, while exposure levels were lower than the HBGVs. These mycotoxins were assessed to be at a safe level of risk for both medium and extreme intake, meaning that the population should not be concerned about the level of exposure. For the exposure levels of individual mycotoxins, mean daily exposure was 0.141 µg/kg bw/day for DON, which was 14.1% of the TDI (1 µg/kg bw/day);, 0.0026 µg/kg bw/day for OTA, which was 16.6% of the TDI (0.0157 µg/kg bw/day);, 0.0168 µg/kg bw/day for ZEA, which was 4.2% of the TDI (0.4 µg/kg bw/day);, 0.212 µg/kg bw/day for FUM, which was 12.8% of the TDI (1.65 µg/kg bw/day);, and 0.0008 µg/kg bw/day for PAT, which was 0.2% of the TDI (0.4 µg/kg bw/day)(Table 3).

For aflatoxin, the detection rate and contamination level in foods were very low. The mean daily exposure for total aflatoxin and aflatoxin B_1 was 0.0011 µg/kg bw/day and that for aflatoxin M_1 was 0.00009 µg/kg bw/day; these levels are lower than the exposure levels in

other countries. The MOE, which compares daily exposure with the no-observed-adverse-effect level(NOAEL) for aflatoxin (0.170 μg/kg bw/day), was used to determine whether aflatoxin exposure posed any risk. Based on the daily exposure to aflatoxins through food (0.0011 μg/kg bw/day), Koreans maintaining an average diet were assessed to have a low possibility of hazardous effects related to aflatoxin exposure. Nevertheless, because aflatoxins are carcinogenic and genotoxic substances, their levels in food should be continuously monitored and reduced until they can be eliminated completely from our diets.

The results of this risk assessment show that when eight mycotoxins with established standards or regulations were investigated in foods susceptible to mycotoxin exposure (agricultural products such as grains and nuts), the detection rates and contamination levels were very low. Domestic exposure levels to these eight mycotoxins were also found to be low compared to the exposure levels in Europe and countries in other parts of the world.

In the exposure assessment, data were collected by face-to-face or phone interviews, in which subjects were asked to recall and record the types, amounts, cooking methods, brand names, eating locations, and eating times of all foods and drinks consumed in the last 24 h or the day before. Thus, extreme intake levels (P95) are calculated as very conservative values that are not encountered in actual exposure situations. Therefore, in exposure assessments, food intake survey methods should be improved to sufficiently reflect real situations, even for cases of high exposure.

In conclusion, at the current stage of assessment, the Korean population is safe from mycotoxins because of the established standards and regulations. Nevertheless, because of the physical nature of mycotoxins, they are affected by environmental factors during the production stage, such as biological factors, temperature, humidity, physical damage, and insect damage. Mycotoxins are also affected, by various other factors at the harvesting, storage, distribution, and processing stages. Because these organisms impact the human body,

it is essential to continually monitor and assess the risk of food-borne mycotoxin contamination levels and detect new mycotoxins.

Because this risk assessment report is based on data collected prior to publication, re-assessment is planned if additional hazard information becomes available or upon the collection of sufficient new monitoring data.

Key words: Mycotoxins, Risk Assessment, Aflatoxin, Deoxynivalenol, Zearalenone, Fumonisin, Ochratoxin, Benchmark dose, Margin of Exposure

Table 3. Daily mycotoxin exposure in each food group (μg/kg bw/day)

Category	Total aflatoxin		Deoxynivalenol		Zearalenone		Ochratoxin A		Fumonisin		Aflatoxin M1		Patulin	
	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
Total	2.6.E-04	1.1.E-03	2.0.E-02	1.4.E-01	4.4.E-03	1.7.E-02	2.7.E-04	2.6.E-03	4.9.E-02	2.1.E-01	3.0.E-06	8.8.E-05	3.7.E-05	8.1.E-04
Grains and grain-based products	1.2.E-04	4.6.E-04	2.0.E-03	7.6.E-02	2.5.E-03	9.7.E-03	5.2.E-05	1.1.E-03	1.7.E-02	1.2.E-01	-	-	-	-
	2.3.E-05	1.0.E-04	3.0.E-03	8.0.E-03	5.1.E-04	9.6.E-04	0.0.E+00	1.1.E-04	2.8.E-02	2.9.E-02	-	-	-	-
Corn and corn-based products	0.0.E+00	5.0.E-06	2.0.E-03	2.0.E-03	6.4.E-05	1.7.E-04	1.0.E-06	8.2.E-05	1.0.E-03	2.0.E-03	-	-	-	-
	0.0.E+00	1.0.E-05	0.0.E+00	1.0.E-03	1.0.E-06	1.4.E-04	0.0.E+00	2.9.E-05	0.0.E+00	1.0.E-03	-	-	-	-
Pulse and pulse-based products	4.0.E-06	1.4.E-05	0.0.E+00	1.0.E-03	1.9.E-05	2.1.E-04	3.9.E-06	3.3.E-05	0.0.E+00	1.0.E-03	-	-	-	-
	0.0.E+00	1.8.E-05	-	-	-	-	1.4.E-06	1.4.E-06	-	-	-	-	-	-
Nuts and nut-based products	9.0.E-06	1.3.E-05	1.0.E-03	1.0.E-03	1.0.E-06	8.8.E-05	4.7.E-06	1.8.E-05	0.0.E+00	0.0.E+00	-	-	-	-

Category	Total aflatoxin		Deoxynivalenol		Zearalenone		Ochratoxin A		Fumonisin		Aflatoxin M1		Patulin	
	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
Cereals	1.0.E-06	4.0.E-06	0.0.E+00	0.0.E+00	8.0.E-06	8.9.E-05	2.9.E-07	1.2.E-05	0.0.E+00	1.0.E-03	-	-	-	-
Nuts and seeds	1.0.E-06	4.0.E-06	0.0.E+00	0.0.E+00	1.8.E-05	6.3.E-05	3.0.E-06	8.4.E-06	0.0.E+00	0.0.E+00	-	-	-	-
Pastes	3.6.E-05	7.8.E-05	1.0.E-03	4.0.E-03	1.6.E-04	7.2.E-04	3.9.E-05	1.5.E-04	0.0.E+00	8.0.E-03	-	-	-	-
Condiments and sauces	1.7.E-05	3.6.E-05	0.0.E+00	0.0.E+00	1.4.E-05	1.3.E-04	2.6.E-05	6.0.E-05	0.0.E+00	0.0.E+00	-	-	-	-
Spices	0.0.E+00	0.0.E+00	-	-	0.0.E+00	0.0.E+00	0.0.E+00	0.0.E+00	0.0.E+00	0.0.E+00	-	-	-	-
Vegetables	2.0.E-06	3.5.E-05	0.0.E+00	0.0.E+00	0.0.E+00	2.9.E-04	0.0.E+00	4.0.E-05	0.0.E+00	0.0.E+00	-	-	-	-
Wheat flours	2.0.E-06	1.0.E-05	2.0.E-03	3.0.E-03	3.5.E-04	5.5.E-04	7.1.E-07	4.2.E-05	0.0.E+00	3.0.E-03	-	-	-	-
Fruits (dried)	1.0.E-06	1.2.E-05	0.0.E+00	0.0.E+00	0.0.E+00	1.1.E-04	1.4.E-07	2.0.E-05	0.0.E+00	0.0.E+00	-	-	-	-
Fruits	0.0.E+00	0.0.E+00	-	-	-	-	1.4.E-07	4.3.E-07	-	-	-	-	-	-

Category	Total aflatoxin		Deoxynivalenol		Zearalenone		Ochratoxin A		Fumonisin		Aflatoxin M1		Patulin	
	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
Food for infants and young children*	0.0.E+00	0.0.E+00	0.0.E+00	0.0.E+00	0.0.E+00	9.0.E-06	0.0.E+00	1.7.E-06	0.0.E+00	4.0.E-03	0.0.E+00	1.0.E-06	0.0.E+00	6.0.E-06
Noodles	8.0.E-06	7.1.E-05	1.0.E-03	2.4.E-02	3.2.E-05	8.8.E-04	9.9.E-06	1.4.E-04	0.0.E+00	1.5.E-02	0.0.E+00	4.7.E-05	-	-
Snacks	1.0.E-06	2.5.E-05	1.0.E-03	2.0.E-03	4.8.E-05	4.8.E-04	2.9.E-06	4.4.E-05	1.0.E-03	3.0.E-03	-	-	-	-
Bread and rice cakes	2.0.E-06	3.6.E-05	3.0.E-03	7.0.E-03	1.3.E-05	7.3.E-04	1.5.E-05	1.2.E-04	0.0.E+00	7.0.E-03	-	-	-	-
Tofu and *muk*	1.8.E-05	4.3.E-05	2.0.E-03	6.0.E-03	-	-	2.9.E-07	1.2.E-04	-	-	-	-	-	-
Coffee	0.0.E+00	1.1.E-05	0.0.E+00	1.0.E-03	1.0.E-06	1.4.E-04	5.7.E-06	1.1.E-04	0.0.E+00	4.0.E-03	-	-	-	-
Chocolate	0.0.E+00	1.0.E-06	0.0.E+00	0.0.E+00	0.0.E+00	9.0.E-06	0.0.E+00	7.1.E-07	0.0.E+00	0.0.E+00	-	-	-	-
Preserves	-	-	-	-	-	-	1.4.E-07	7.1.E-07	-	-	-	-	-	-
Oils and fats	-	-	-	-	3.0.E-06	4.0.E-06	-	-	0.0.E+00	0.0.E+00	-	-	-	-

Category	Total aflatoxin		Deoxynivalenol		Zearalenone		Ochratoxin A		Fumonisin		Aflatoxin M1		Patulin	
	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
Tea	5.0.E-06	3.2.E-05	0.0.E+00	0.0.E+00	3.4.E-05	3.6.E-05	7.1.E-05	7.2.E-05	0.0.E+00	0.0.E+00	-	-	-	-
Alcohol	-	-	-	-	-	-	1.4.E-06	3.4.E-05	-	-	-	-	0.0.E+00	2.0.E-05
Beverages	1.0.E-06	1.9.E-05	0.0.E+00	3.0.E-03	2.2.E-04	5.9.E-04	1.3.E-05	1.6.E-04	0.0.E+00	9.0.E-03	-	-	3.7.E-05	7.9.E-04
Raw processed foods	0.0.E+00	1.0.E-06	0.0.E+00	0.0.E+00	6.6.E-05	8.7.E-05	1.0.E-06	4.9.E-06	0.0.E+00	0.0.E+00	-	-	-	-
Instant/convenience foods	0.0.E+00	6.0.E-06	0.0.E+00	1.0.E-03	1.0.E-06	5.3.E-05	8.6.E-07	6.4.E-06	0.0.E+00	0.0.E+00	-	-	-	-
Starches	0.0.E+00	1.0.E-06	-	-	-	-	0.0.E+00	6.3.E-06	0.0.E+00	0.0.E+00	-	-	-	-
Other foods	1.0.E-06	7.0.E-06	0.0.E+00	0.0.E+00	2.5.E-04	5.2.E-04	1.5.E-05	5.5.E-05	0.0.E+00	5.0.E-03	-	-	-	-
Processed milk products	7.0.E-06	4.7.E-05	-	-	0.0.E+00	1.3.E-05	0.0.E+00	1.3.E-06	0.0.E+00	0.0.E+00	3.0.E-06	3.9.E-05	-	-
Ingredients for use in medicines and foods	-	-	-	-	-	-	-	-	0.0.E+00	0.0.E+00	-	-	-	-