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Mini Review

Significance of regulation limits in mycotoxin contamination in Asia and risk management programs at the national level

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ABSTRACT

Mycotoxins are the secondary metabolites produced from toxigenic fungi recognized as major food and feed contaminants. They are a source of grave concern in food contamination, resulting in mycotoxicosis in humans and animals. To date, many regulations on the allowable levels of each mycotoxin have been established in several countries. Consumers and food producers expect that toxin contamination in food and feed, based on government regulations and guideline levels, should have no adverse consequences on human and animal health. This review is an extension of the discussions during the international seminar entitled *Risk Assessment and Risk Management of Mycotoxins for Food Safety in Asia*, which was jointly organized by Kasetsart University (Thailand) and the Food and Fertilizer Technology Center for the Asian and Pacific Region (Taiwan) and held in Chonburi, Thailand, in September 2011. In this review, we discuss the recent findings on mycotoxins in food and feed, with emphasis on aflatoxins, fumonisins, ochratoxins, and zearalenone, as well as the national management programs that will supply a wider knowledge base for establishing appropriate control measures for mycotoxins in Asian countries. However, we believe that continuing support from national governments and regional communities is essential to encourage and fund activities that contribute to a reliable exposure risk assessment and risk management of mycotoxins in the region, and also to improve our understanding and practices in order to protect consumers from the health threat posed by mycotoxin contamination.

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1. Introduction

Mycotoxins are the secondary metabolites produced from toxigenic fungi recognized as major food and feed contaminants. They are a source of grave concern in food contamination, resulting in mycotoxicosis in humans and animals. Typically, toxin production is influenced by moisture, time, temperature, and food or feed substrates. Contamination can occur throughout the food chain—from the field, during harvesting, processing, storage, transportation, and consumption [1]. For raw materials, preharvest contamination of mycotoxins is the most difficult part in risk management. Regarding food safety issues, food and feeds absolutely free from fungi and mycotoxins are needed everywhere to prevent health hazards and to secure the international food trade.

To date, many countries have established regulatory controls over the levels of each mycotoxin—a measure that could help reduce toxin intake by removing the offending products from the market. Both consumers and food producers expect that toxin contamination in food and feed, based on government regulations and guideline levels, will have no adverse consequences on human and animal health. Based on the toxigenicity of several mycotoxins, regulatory levels have been set by many national governments and adopted for use in national and international food trade. Internationally, Codex, the European Union (EU), and other regional organizations have issued a number of decrees mandating the maximum levels of mycotoxins in foods and feeds according to the provisional maximum tolerable daily intake, which was used as the guideline for controlling contamination by mycotoxins, and preventing and reducing toxin contamination for the safety of consumers. The Codex Alimentarius Commission (CAC) was founded in 1963 by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) to develop CODEX standards, guidelines, and other documents pertaining to foods such as the *Code of Practice* for protecting the health of consumers and ensuring fair practices in food trade. The CAC comprises more than 180 member countries, representing 99% of the world's population. The Codex Committee on Food Additives and Contaminants has issued codes of practice for the prevention and reduction of mycotoxin contamination in several foods and feeds—for example, codes of practice for ochratoxin A, zearalenone, fumonisins, and tricothecenes in cereals (CAC/RCP 51-2003); codes of practice for patulin in apple juice and apple juice ingredients in other beverages (CAC/RCP 50-2003); codes of practice for aflatoxin contamination in peanuts (CAC/RCP 55-2004), treenuts (CAC/RCP 59-2005), and dried figs (CAC/RCP 65-2008); codes of practice for ochratoxin A in wine (CAC/RCP 63-2007) and coffee (CAC/RCP 69-2009); as well as codes of practice for aflatoxin B1 in raw materials and feeding stuffs for milk-producing animals (CAC/RCP 45-1997) [2].

As food producers and government control authorities in Asian countries are directing their efforts toward the implementation of a correct and reliable evaluation of the real status of mycotoxin contamination in food commodities in order to evaluate the regulation limits of mycotoxins in each food and feed, the first international seminar on risk assessment and risk management of mycotoxins for food safety in Asia was held in September 2011, through the joint efforts of Kasetsart University (Thailand) and the Food and Fertilizer Technology Center for the Asian and Pacific Region (FFTC; Taiwan), in order to share and exchange relevant knowledge among countries. This paper pointed out two interesting issues: the correlation between the occurrence of mycotoxin contamination in food and feed commodities and current regulation limits of each country as well as the national management programs, which were discussed by 15 invited speakers from seven countries (Taiwan, Japan, Korea, Philippines, Malaysia, Indonesia, and Thailand). The data on mycotoxin occurrence from 2005 up to the present were also evaluated.

2. Occurrence of major mycotoxin contamination in Asia and significance of regulation limits

2.1. *Aflatoxins*

Aflatoxins are hepatocarcinogenic toxins consisting of three main metabolites, aflatoxin B, G, and M, which belong to difurocoumarin-derivative compounds [3–5]. Different *Aspergillus* species produce different derivatives. *Aspergillus flavus* produces only aflatoxin B, whereas *Aspergillus parasiticus* and *Aspergillus nomius* produce aflatoxins B and G. Afaltoxins B and G are mostly found in dried fruits, spices, and cereals such as corn, peanuts, nuts, and copra. Aflatoxins M1 and M2 are the hydroxylated metabolites of aflatoxins B_1 and B_2 and can be found in milk or milk products obtained from livestock that have ingested contaminated feeds [6,7].

Among the mycotoxins, the toxic effects of aflatoxins vary widely. Aflatoxins cause liver cancer and enhanced carcinogenic potency with hepatitis B infection in certain individuals [8,9]. It is the most potent hepatocarcinogen known [10]. In 1960, aflatoxin outbreaks in Turkey and England have resulted in 100,000 deaths. Because of these incidents, it was called the Turkey-X disease. Later, in 1961, another outbreak of aflatoxins occurred in ducks in Kenya, Uganda, and West Africa. Recently, acute aflatoxicosis caused more than 123 deaths in Kenya [11]. From 1991 to 2009 in Japan, more than 1500 violation cases were reported for aflatoxin B1 contamination in imported foods from plant sources at the level of 10–4918 μg/kg [12].

Moisture and oxygen content are the most important environmental factors affecting aflatoxin production. Typically, aflatoxin B is produced at 11–37 °C, whereas aflatoxin G production usually occurs at 28 °C [13]. Therefore, because of the increased continental and global changes in surface temperature during the past 10 years, in the temperate zone, elevated temperatures may facilitate the growth of fungi that thrive in warmer climate such as *Aspergillus* spp., causing an increased production of aflatoxins. However, in general, increase in temperature does not have much of an effect on these fungi [2].

With the possible changes (e.g., climate) in mycotoxin problems in various kinds of food commodities such as peanuts, corns, cereals, animal foods, milk, and dairy products, the risk assessment of aflatoxins was performed systematically in order to form the basis for regulations and control. Aflatoxin B and G contamination has been the biggest source of concern for corns and peanuts from 48 countries all over the world, and national regulation limits have thus been established based on national food consumption and concentration data as well as international nutritional and toxicological reference values [2,9]. Typically, regulatory standards set by the Codex specify 15 μg/kg for total aflatoxins in peanuts and 0.5 μg/kg for aflatoxin M1 in milk, whereas the US Food and Drug Administration (FDA) has placed the limit at 20 ppb [1]. However, different regulations have been established by each Asian country (Table 1). Compared to a different survey of aflatoxin contamination in various food and feed commodities among Asian countries (Table 2), some of the analyzed samples contain aflatoxin levels that exceed the Codex regulation limit (15 ppb). Peanut and corn are the major contaminated products in almost all countries, especially exported raw peanut, which has become an issue of contention across countries [14]. In Thailand, the percentage of major aflatoxin contamination was observed in peanuts (51.4%), milk and dairy products (95.56%), dried seafood (58.6%), poultry tissue (48.67%) [15], and corn (54.39%) [16]. These data suggest that the government should exert more efforts or establish a novel prevention program in controlling aflatoxin contamination in these sources.

2.2. *Fumonisins*

Fumonisins were discovered in 1988 following an outbreak of equine encephalomalacia in South Africa in 1970 [17]. Later in 1989 and 1990, fatal outbreaks of equine leukomalacia and porcine prenatal and neonatal mortality and pulmonary edema occurred in the United States (US) [18]. In humans,

Table 1 – Regulation limits of aflatoxin subtypes and total aflatoxins in Asian countries.

Country	Types of aflatoxins	Maximum limit (ppb)	Food and feed commodities	Refs
China	B1	20	Maize, peanut	[2]
	B1, M1	0	Infant foods	[12]
	M1	0.5	n/a	[12]
Hong Kong	Total	20	Peanut, peanut products	[2,12]
	Total	15	Other foods	[2,12]
India	Total	30	n/a	[2]
	B1	30	All	[2]
Indonesia	Total	50	Corn feed	[64]
	Total	35	All foods	[64]
	B1	20	All foods	[64]
	B1/total	15/20	Peanut, corn and their products	[64]
	M1	5	Dried milk and related products	[64]
	M1	0.5	Milk, drink milk products, fermented milk and rennin hydrolyzed milk products, concentrated milk, cream, cheese, pudding, yogurt, whey and their products	[64]
Japan	Total	10	All foods	[2,72]
	B1	10	Rice	[2,12]
	B1	5	Other grains	[2]
South Korea	B1	10	Grains, cereal products, dried fruits, Meju, and streamed rice	[12,45]
	B1	0.1	Baby foods	[45]
	B2, G1, and G2	15	Grains, cereal products, dried fruits, Meju, streamed rice, and baby foods	[45]
	M1	0.5	Raw milks and milks prior to manufacturing processing	[12,45]
Malaysia	Total	35	All	[2,12]
Philippines	Total	20	Human foods	[12,70]
	B1	20	Coconut, peanut products (export)	[2]
	M1	0.5	Milk	[70]
Singapore	Total	5	All	[12]
	M1	0.5	n/a	[12]
Sri Lanka	Total	30	All	[2,12]
	M1	1	Infant foods	[12]
Taiwan	Total	15	Peanut, corn	[73,74]
	Total	10	Rice, sorghum, beans, wheat products, nuts, edible oils, and other foods	[73,74]
	Total	0	Infant foods	[12]
	M1	5	Milk powder	[74]
	M1	0.5	Fresh milk	[12,74]
Thailand	Total	20	All	[2,12]
Vietnam	Total	10	All	[12]
	M1	0.5	All	[12]

n/a = not available.

Table 2 – Examples of total aflatoxins contamination in food and feed commodities during 2006–2011 reported in literature and presented at the FFTC–KU 2011 mycotoxin conference.

Commodity	Country	Range of contamination (ppb)	Average level (ppb)	Refs
Assorted nuts (seasoned)	South Korea	7.89	7.89[a]	[75]
Banana chips	Philippines	<5[b]		[70]
Cereals	Taiwan	ND–4.8[c]		[76]
Chili	Malaysia	0.2–79.71[a]		[77]
Coconut meal	Thailand	6.10–229.00	73.36[a]	[78]
Coconut and products	Philippines	<5–32.5[b]		[70]
Corn flakes, popcorn, corn puff, gritted corn	Indonesia	<20		[64]
Corn gluten meal	Thailand	2.50–302.60	55.39[d]	[78]
Corn products	Philippines	<5–495.70[b]		[70]
Egg battered peanut (kacang telor)	Indonesia	0.50–2.90		[64]
Feed—cattle	Thailand	1.25–21.20	7.21[d]	[78]
Feed—dairy cow	Thailand	37.47–201.38 (aflatoxin B_1)		[15]
Feed—fish	Thailand	2.80–80.10	22.14[d]	[78]
Feed—shrimp	Thailand	1.50–22.10	8.97[d]	[78]
Fish powder	Thailand	1.40–169.75	20.44[d]	[78]
Fried battered peanut (peyek)	Indonesia	1.20–4.40		[64]
Fried peanut (kacang goreng)	Indonesia	1.00–2.30		[64]
Hairy basil seed	Thailand	1.30–50.20	5.11[d]	[78]
Job's tear	Thailand	2.10–95.90	12.12[d]	[78]
Maize	Thailand	1.20–380.00	60.63[d]	[78]
Milk—commercial milk	Japan	0.0169–0.019 (Aflatoxin M1)	0.073[a]	[72]
	Taiwan	ND–0.038[e] (Aflatoxin M1)		[76]
Milk—powdered milk	Thailand	ND–0.065[a] (Aflatoxin M1)		[72]
Milk—raw milk	Thailand	0.16–0.75 (Aflatoxin M_1)		[15]
Milk—school milk	Thailand	<0.5 max 0.114)[e]		[79]
Nuts and coated cracker nuts (cashew, walnut, pili)	Philippines	<5[b]		[70]
Peanut	Thailand	2.20–171.30	31.54 [d]	[78]
	Malaysia	0–103.23	11.28[a]	[80]
Peanut and products	Philippines	<5–16,000[a]		[70]
Peanut butter	South Korea	7.03–7.68	7.36[a]	[75]
Peanut—raw	South Korea	0.20	0.20[a]	[75]
Peanut—roasted	South Korea	2.00–28.4	10.67[a]	[75]
Peanut with coconut sugar cake (ampyang)	Indonesia	1.50–2.80		[64]
Peanut sauce (bumbu pecel)	Indonesia	0.5–19.5 (max 100)		[64]
Peanut—sweetened peanut (enting gepuk)	Indonesia	<20–21.2		[64]
Pepper (seeds and powder)	Malaysia	0.1–25.8[a]		[81]
Rice—black glutinous rice	Thailand	8.00–38.80	18.21[d]	[78]
Rice—bran	Thailand	1.80–81.80	21.41[d]	[78]
Rice—brown rice	Thailand	1.70–68.50	13.90[d]	[78]
	Philippines		0.39[e]	[68]
	China		0.88[a]	[82]
Rice, imported	Philippines	<5–8.66[b]		[68,70]
Rice, marketed	Vietnam		3.31 (max 29.8)[a]	[83]
Rice—polished, imported	Japan	0.1–0.3		[68]
Rice—white rice	Thailand	0.80–12.60	3.01[d]	[78]
Rice—white glutinous rice	Thailand	1.20–14.40	5.74[d]	[78]
Soybean meal	Thailand	1.20–17.60	5.88[d]	[78]
Wheat	Thailand	2.40–30.00	12.23[d]	[78]
Wheat flour	Thailand	1.70–11.76	5.56[d]	[78]

FFTC-KU = Food and Fertilizer Technology Center for the Asian and Pacific Region-Kasetsart University; ND = not detected.
[a] Analyzed with high performance liquid chromatography (HPLC).
[b] Analyzed with thin layer chromatography.
[c] Analyzed with enzyme-linked immunosorbent assay (ELISA).
[d] Analyzed with DOA-Aflatoxin ELISA test kit.
[e] Analyzed with immunoaffinity chromatography-HPLC.

fumonisins may be the etiological agent of esophageal carcinoma [19], and have been found to interfere with cellular folate uptake [20] and increase the rate of neural tube defect [21].

Fumonisins can be divided into four structurally distinct groups—designated A, B, C, and P—of which fumonisin B1, which was isolated in 1988, is the most important form [22]. These mycotoxins are produced by at least 11 species of the fungus *Fusarium*. The maize pathogens *Fusarium verticillioides* (or named *Fusarium moniliforme*) and *Fusarium proliferatum* are the main fungi producing fumonisins and are principally found in maize in the field. Basically, *F. moniliforme* exhibits good growth at the temperature range of 3–37 °C, with the optimum rate noted at 25 °C. In temperate zones under changing climate conditions, high temperature may decrease fungi that favor cold climate such as *Fusarium* and *Penicillium*. However, in tropical zones, increase in temperature may not decrease such fungi but could lead to a lower contamination level than that in temperate countries [2,5,23,24].

Biomin's mycotoxin survey report provided a global overview of mycotoxin occurrence in a diverse variety of materials, from cereals to processed by-products [25]. Recently, the annual report between January 2011 and December 2011 has been launched. A total of 4,327 samples were analyzed, and 13,854 analyses were completed for aflatoxins, zearalenone, deoxynivalenol (DON), fumonisins, and ochratoxin A (OTA), which are important in agriculture and animal production (Fig. 1). In Asia, the prevalence of mycotoxins is different from that in other geographical regions according to the percentage of positive samples. Regarding the regional difference of fumonisins, the highest prevalence is observed in South America with a positive rate of 76% [average level of 1501 μg/kg (ppb)] [25]. In Asia, the positive rate of fumonisins was 52%, with an average level of 936 μg/kg [25]. Among Asian regions, South Asia has the highest positive rate, which was 56%. However, there is no significant difference in positive fumonisins sample between Southeast Asia (55%) and North Asia (51%) [25].

As fumonisins B1 and B2 are the most potent esophageal carcinogens, many countries are concerned mostly with these two subtypes. Even the Codex has not established the maximum limit for fumonisins yet. Large international markets, such as China, Japan, India, Russia, and Latin American countries, have set no specific values for them. Some Asian countries have established their own regulation limits for fumonisins, which facilitates their international trade (Table 3). However, the US FDA has issued advisory limits on fumonisins in human foods [1]. Such advisory limits include 2,000 ppb for degermed dry milled corn products such as flaking grits, corn grits, corn meal, and corn flour with fat content of <2.25% dry weight basis; 4,000 ppb for whole or partially degermed dry milled corn products such as flaking grits, corn grits, corn meal, and corn flour with fat content of >2.25% dry weight basis; 4,000 ppb for dry milled corn bran, cleaned corn intended for mass production; and 3,000 ppb for cleaned corn intended for popcorn [1]. However, these levels are different from those set by EU regulations for fumonisins: 2,000 ppb for unprocessed maize; 1,000 ppb for maize grits, meal, and flour; and 200 ppb for processed maize-based foods for infants and young children and baby food [1]. Other maize-based foods for direct consumption, except maize grits, meal, flour, and processed maize-based foods for infants and young

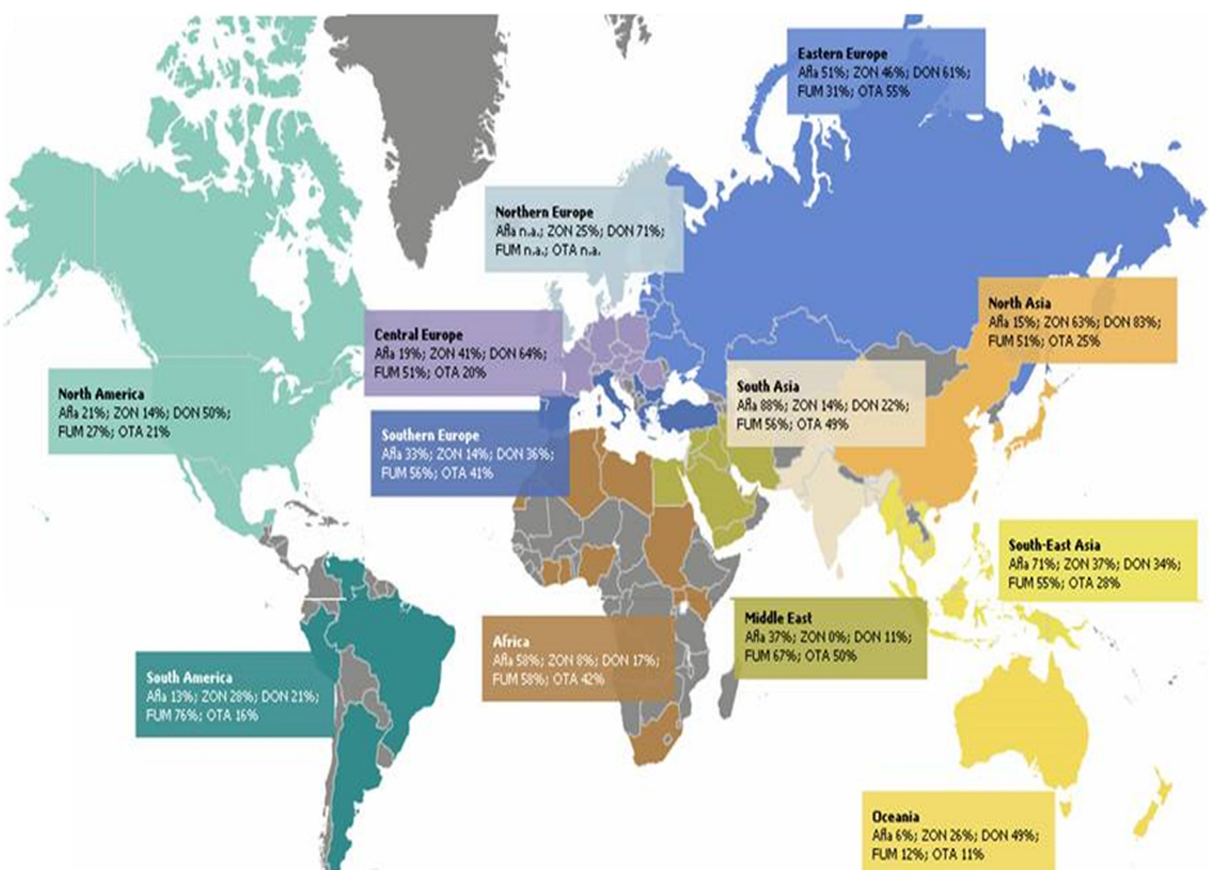

Fig. 1 – Prevalence of mycotoxins across the world between January and December 2011 [25]. Afla = aflatoxins; DON = deoxynivalenol; FUM = fumonisins; OTA = ochratoxins; ZON = zearalenone.

Table 3 – Regulation limits of fumonisins (B1 and B2) in some Asian countries.

Country	Maximum limit (ppb)	Food and feed commodities	Refs
Indonesia	2000	Corn (raw material)	[64]
	1000	Corn foods products, e.g., popcorn, corn chips	[64]
South Korea	1000	Grain products, cereals, processed corn products for popcorn, confectionaries (contain >50% corns)	[45]
	2000	Corn processed food, corn powder	[45]
	4000	Corn	[45]

children, and baby food, were regulated at 400 ppb [1]. Nevertheless, from those maximum limits advised, corn represents the major worldwide target to establish a prevention program to deal with fumonisin contamination.

For feed ingredients and finished feed collected from Southeast Asian countries (Indonesia, Malaysia, Philippines, Thailand, and Vietnam), fumonisins B1 was found to contaminate 81% of maize samples, and many of them exceeded the maximum limit set by their respective countries [26] (Table 4). In Thailand, the contamination level at more than 1,000 ppb of fumonisin increased dramatically from 26.40% in 2008 to 37.70% in 2011 in raw agricultural materials; and from 2.89% in 2008 to 15.38% in 2011 in finished feeds. In particular, the high level of fumonisin contamination in raw materials was noted in corn and distiller dried grains with soluble [15]. All lines of evidence could frame the limitations of recent contamination control programs in each country and aid policy making in setting safe and feasible regulatory standards and further efficient mycotoxins management programs.

2.3. *Ochratoxins*

OTAs comprise a family of mycotoxins that includes ochratoxin A, which is the most prevalent of all ochratoxins. They are the secondary fungal metabolites of *Penicillium* in the temperate climate zone and *Aspergillus* species in the tropical climate zone. *Penicillium verrucosum*, *Aspergillus ochraceus*, and *Aspergillus ostanius* mainly produce ochratoxins mostly found in barley and stored cereals [27]. The toxic effect of ochratoxins is acute, and could lead to chronic kidney cell damage and impaired function. Females are more sensitive to these toxins than males [28,29]. During testing of the toxicological effect of OTAs using laboratory animals, nephrotoxic, hepatotoxic, and teratogenic effects were observed [30]. Moreover, OTA is a carcinogenic agent associated with the upper urinary tract [31] and testicle [32], as it was first found in corn in South Africa in 1960 followed by the Balkan nephropathy outbreaks, a fatal chronic renal disease, in Bulgaria [33].

OTA is found mostly in stored grains. To reduce the chance of OTA exposure in humans and animals, a uniform maximum level of 5–20 ppb was set around the world and among Asian countries (Table 5). Compared to the EU criteria, the maximum limits were set at 2 μg/kg for wine and grape juice, 5 μg/kg for raw cereal grains, 3 μg/kg for processed cereal products, 5 μg/kg for roasted coffee, and 10 μg/kg for instant coffee and raisins [1]. This similarity was also observed.

Beer, cereals, coffee, pork meat, and cocoa products are the main food carriers of OTA [34,35] (Table 6). In 2011, the highest pre valence of OTA contamination in foods and feeds occurred

Table 4 – Fumonisins contamination in food and feed commodities in Asian countries.

Commodity	Country	Range of contamination (ppb)	Refs
Corn flour	South Korea	90.89–439.67[a]	[84]
Corn, corn products	South Korea	10–850 (B1)[a] ND–140 (B2)[a] ND–60 (B3)[a]	[45]
Cereal and cereal products	South Korea	ND–50 (B1)[a] ND–20 (B2)[a] ND–20 (B3)[a]	[45]
Dried corn	South Korea	121.98–268.12[a]	[85]
Job's tear, germinated brown rice, brown rice, snack, corn flakes	Thailand	ND[b]	[86]
Maize	China, India, Indonesia, Philippines, Thailand, Vietnam	0.01–155[c]	[5]
Maize flour	China, India, Japan, Thailand, Vietnam	0.06–2.60[c]	[5]
Maize snacks and products	Japan, Taiwan	0.07–2.39[c]	[5]
Maize feed	South Korea, Thailand	0.05–1.59[c]	[5]

ND = not detected.
[a] Analyzed with LC/FLD (liquid chromatography with fluorescence detection).
[b] Analyzed with HPLC-FLD (high performance liquid chromatography with fluorescence detection).
[c] Analytical method not mentioned.

Table 5 – Regulation limits of ochratoxins in some Asian countries.

Country	Maximum limit (ppb)	Food and feed commodities	Refs
Indonesia	20	Spices	[64]
	10	Instant coffee	[64]
	5	Cereals (rice, corn, sorghum, wheat) and their products and coffee	[64]
South Korea	20	Meju	[45]
	10	Instant coffee and raisins	[45]
	7	Red pepper powder	[45]
	5	Grains and their processed food (grinding, cutting, etc.), coffee beans, and roasted coffee	[45]
	0.5	Baby foods for infants and young children	[45]
Singapore	2.5	Cereal, raw coffee beans, and roasted coffee beans	[1]
Taiwan	5	Rice and wheat products	[74,76]

in South Asia with a positive rate of 49%, which is twice more than that found in North Asia (25%) and Southeast Asia (28%; Fig. 1) [25]. However, the risk of ochratoxin contamination in raw materials varies with seasons year by year [36]. Therefore, monitoring of the contamination status should be continued especially when the climate changes continuously.

2.4. *Zearalenone*

Zearalenone, previously named F2 toxin, is an estrogenic mycotoxin synthesized by *Fusarium* fungi including *Fusarium graminearum*, *Fusarium culmorum*, *Fusarium cerealis*, *Fusarium equiseti*, and *Fusarium crookwellense*, with contamination occurring mainly in maize, wheat, and barley fields [2]. These fungi are common soil fungi mostly found in warm and temperate areas. Wheat and rice are the preferred substrates for zearalenone production, whereas oat and barley provide very low toxin yield and peas yield none at all [37,38]. Estrogenic syndrome is the major toxic effect of zearalenone as its structure resembles that of 17-beta-estradiol, an estrogen hormone. Hyperestrogen, vulvovaginitis, and estrogenic responses from zearalenone are observed in estrogenic target cells [39]. An amount of 1 mg/kg in feed can cause estrus in swine [40]. Contamination in food and feed stuffs has been reported annually. From Biomin's mycotoxin report 2011, the highest contamination of zearalenone was found in Asia with 53% of positive samples compared to 26%, 35%, 14%, 28%, 0%, and 8% reported for Oceania, Europe, North America, South America, Middle East, and Africa, respectively [25] (Fig. 1). In Asia, North Asia showed the highest contamination (63%), Southeast Asia was second (37%), and South Asia had the lowest rate (4%) [25] (Fig. 1). However, the average amount of zearalenone contamination in Asia was 129 μg/kg, which was still within the range of the maximum limits regulated in Asian countries (Table 7). Although the maximum limit of zearalenone in food and feed stuffs has not been established

Table 6 – Ochratoxins contamination in food and feed commodities in Asian countries.

Commodity	Country	Range of contamination (ppb)	Average level (ppb)	Refs
Barley	Taiwan		35 ± 3^a	[76]
Black bean	Taiwan		74 ± 6^a	[76]
Buckwheat	Taiwan		$60^b/144 \pm 8^a$	[76]
Chili	Malaysia	$0.2–101.24^c$		[77]
Coffee	Taiwan		10.97 ± 0.27^a	[76]
Coffee mix	South Korea		4.186^d	[36]
Corn	Thailand		2.29^b	[87]
Dried fig	South Korea		0.667^d	[36]
Dried grape fruit	South Korea		6.233^d	[36]
Pepper (seeds and powder)	Malaysia	$0.2–33^c$		[81]
Perilla seeds	South Korea		10.261^d	[36]
Pork meat and ham products	South Korea	$0.06–0.075^d$		[36]
Red pepper powder	South Korea		7.153^d	[36]
Rice, barley, wheat, corn and mixed cereal	South Korea	$0.045–5.235^d$		[36]
Roasted coffee	Taiwan		$220^b/160 \pm 9^a$	[76]
Soybean and soybean products	South Korea	$0.03–15.238^d$		[36]
Wheat	Taiwan		84 ± 4^a	[76]

[a] Analyzed with enzyme-linked immunosorbent assay.
[b] Analyzed with high performance liquid chromatography (HPLC).
[c] Analyzed with HPLC-FLD (High Performance Liquid Chromatography with Fluorescence detection).
[d] Analyzed with not mentioned.

Table 7 – Regulation limits of zearalenone in Asian countries.

Countries	Maximum limit (ppb)	Food and feed commodities	Refs
Indonesia	Not detectable	Maize	[1]
Japan	1000	Compound feeds	[1]
South Korea	200	Grains and processed grain foods	[45]
	50	Confectionaries	[45]
	20	Baby foods	[45]
Thailand	30–1000	All foods	[2]

in all Asian countries, EU regulations could be used as a principle reference in the validation of national toxin prevention programs to reduce the risk of toxin contamination throughout the food chain. The European committee regulated that the maximum level of zearalenone in corn should be up to 200 ppb [41] in terms of unprocessed maize. For other unprocessed cereals, 100 ppb is the limit. The limits for cereal snacks, breakfast cereals and processed cereal-based foods, and baby foods were set at 50 ppb, 50 ppb, and 20 ppb, respectively [42]. By contrast, there is no US legislation for zearalenone imposed.

The regulation limits for zearalenone established in various Asian countries are relatively diverse and different from those set by EU regulations (Table 7). However, the occurrence of this toxin in processed food was largely lower than that found in the EU and in each country's regulation limits except in Indonesia, which showed a slightly higher level (Table 8).

2.5. *Deoxynivalenol*

DON is a trichothecene mycotoxin produced by several plant pathogenic fungi, especially *F graminearum* and *F culmorum* [43]. DON is commonly found in wheat, maize, rye, rice, oat, and barley that are infected with *Fusarium* head blight [43]. DON is also known as "vomitoxin," and its presence in foods can cause clinical or subclinical manifestations in humans and animals. The toxicity of DON mainly affects the immune system and the gastrointestinal tract. A low dose ingestion of DON causes anorexia, reduced growth, and reduced nutritional efficiency, whereas a high dose causes acute effects—vomiting, rectal bleeding, and diarrhea. It was also demonstrated that DON has long-term toxic effects on the immune system, growth, and reproduction [44].

Maximum limits for DON are commonly established for products such as unprocessed cereals and cereal products (i.e., pasta and bread). For the EU, the maximum limits of DON are set at 500 ppb and 750 ppb for cereal products as consumed and other cereal products at retail storage, and flour used as raw material in food products, respectively [1]. For other countries, maximum limits are mainly set for cereals, especially wheat, in relation to EU and international recommendations. However, for Asian countries, only South Korea, Japan, and Indonesia have set their own regulation limits for DON in food commodities (Table 9) [1,45,46]. Table 10 shows the occurrence of DON in food commodities in some Asian countries. Fortunately, most of the DON contaminated levels did not exceed the regulation limits. Therefore, based on data of DON contaminated levels together with their consumption rates, the estimated daily intake of DON did not exceed the Provisional Maximum Tolerable Daily Intake in all age groups and both genders in Asian populations [47–49].

2.6. *T-2 toxin*

T-2 toxin is a member of trichothecene metabolites that belong to type A nonmacrocyclic trichothecenes. T-2 toxin was discovered in 1968 from *F tricinctum* [50]. Aside from this species, *Fusarium sporotrichioides*, *F. culmorum*, and *Fusarium poae* can also produce T-2 toxins on cereal grains especially in cold climate or wet conditions [12,51,52]. T-2 toxin and other trichothecenes can cause acute and chronic toxicity, disrupting DNA and RNA synthesis, which affects the production of lymphoid and erythroid cells and induces cell apoptosis [45]. These toxins can also reduce antibody levels and attack the immune system [45]. In experimental animals and livestock, vomiting, diarrhea, loss of appetite, weight loss, and hemorrhages can be the results of T-2 toxin exposure [41].

T-2 toxin tends to be found in cereal products such as wheat, barley, maize, and oats rather than other products [12]. Although T-2 toxin has been found less frequently than other

Table 8 – Zearalenone contamination in food and feed commodities in Asian countries.

Commodity	Countries	Range of contamination (ppb)	Refs
Corn and poultry feeds	Indonesia	5.5–526[a]	[88]
Corn samples	Taiwan	7.9–9.0[b]/8.1–8.9[c]	[89]
Dried confectioneries, breads rice cakes, noodles, snacks, biscuits, other cereal products	South Korea	5.38–53.76[d]	[45]
Infant formula, biscuit (wheat base), breakfast cereals	South Korea	4.3–18.2[d]	[90]
Instant noodle	South Korea	0[d]	[90]
Mixed cereals, oat, rice, wheat	Taiwan	0[b,c]	[89]
Rice	South Korea	21.7–47[b]	[91]

[a] Analyzed with high performance liquid chromatography (HPLC).
[b] Analyzed with HPLC-FLD (High Performance Liquid Chromatography with Fluorescence detection).
[c] Analyzed with LC-mass spectrometry (MS)/MS.
[d] Analytical method not mentioned.

Table 9 – Regulation limits of deoxynivalenol in some Asian countries.

Countries	Maximum limit (ppb)	Food and feed commodities	Refs
Indonesia	1,000	Maize, wheat	[46]
	750	Pasta, noodle, and related products	[46]
	500	Ready-to-eat products (processed flour, pastry, bread, biscuit, snack)	[46]
Japan	1,100	Wheat	[1]
South Korea	1,000	Grain and their processed foods	[45]
	2,000	Corn and their processed foods	[45]
	500	Cereals	[45]

trichothecenes in natural products, its toxicity seems to be the highest [53]. However, T-2 toxin was reported more frequently in Europe than in the United States [54]. Thus, most of the updated reports we found are on T-2 toxin surveyed in products in Europe where oats are highly contaminated at high concentrations, whereas maize is moderately contaminated and wheat is contaminated at low concentration levels but occurred more frequently [55]. Similar to feed and food products, by-products from oat tend to be highly contaminated with T-2 toxins compared to products from other cereals [56]. For example, the maximum T-2 toxin concentration detected in oat food products in Europe was 266 ppb, whereas only 8.4 ppb was detected in maize food products [55]. However, there has been no limitation level set for T-2 toxins in European countries yet. More data are required on the effect of food processing and other factors that can increase or reduce the presence of T-2 toxin in cereals and cereal products [56].

At present, several countries have already issued regulation limits for T-2 toxins in feed and food products. Russia has established a maximum limit of 100 μg/kg for food grains, including wheat, rye, triticale, oats, barley, millet, buckwheat, rice, corn, sorgo, oatmeal, flakes, and wheat flour including pasta. However, products containing cereals for pregnant and nursing women and children 3–14 years old should not contain T-2 toxins within the limit of detection of 50 μg/kg [57]. Among non-EU countries, Ukraine has set a limit of 200 μg/kg in combined feed for layers and broilers, and 250 μg/kg in combined feed for calves and older cattle fed for beef [58]. In Asia, no regulation limits have been set for T-2 toxins, except in China, which established the regulation limit in complete feed at 80 μg/kg [58].

Because several factors such as year-climate, harvesting procedures, and storage conditions can influence T-2 toxin contamination in different regions [12], the concern of public health, the presence of T-2 toxins in cereal grains, feed, and food products, and recent risk assessment need to be prioritized and completed in Asia in the near future. Lack of strong recent information precluded the possibility of establishing appropriate limits for specific products in each country. However, in the first conference on risk assessment and risk management of mycotoxins for food safety in Asia (Thailand, 2011), more T-2 toxin occurrence reports came from South Korea, Japan, and Thailand (Table 11). In Japan, during 2001–2005, T-2 toxin was reported to be almost 40% in milo, which contains malted wheat or barley as the main composition, 12% in formula feed, and 9% in corn, whereas none was detected in other feed grains and commercial products [12]. From a recent report (2012), the highest incidence of T-2 toxin contamination in South Korea was detected in corn at the maximum level of 41.5 μg/kg, and the mean of all samples (brown rice, barley, mixed grains, corn, wheat, and wheat flour) was pegged at 1.5–4.1 μg/kg [59].

3. Regulations and management for mycotoxin in Asian countries

Mycotoxin contamination of foodstuffs has become a top priority issue in human health. In terms of regulatory aspects, since the discovery of the aflatoxins in the 1960s, regulations have been established in many countries to protect consumers from intake of harmful mycotoxin-contaminated

Table 10 – Deoxynivalenol concentration in food commodities in Asian countries.

Commodity	Countries	Range of contamination (ppb)[a]	Average amount (ppb)	Refs
Breads	Thailand	140–1,130	370	[47]
Cereals	Thailand	130–390	240	[47]
Cereals and cereal products	South Korea	–	240	[45]
Instant noodles	Malaysia	ND–970	561	[48]
	Thailand	ND–913	614	[48]
	Indonesia	786–886	833	[48]
Maize kernels and maize products	Indonesia	47–348	125	[46]
Noodles	Thailand	170–350	260	[47]
Yellow alkaline noodles	Malaysia	ND–124.4	514	[48]

ND = not detected.

[a] Analyzed with high performance liquid chromatography.

Table 11 – T-2 toxin contamination in food and feed commodities in Asian countries.

Commodity	Countries	Range of contamination (ppb)	Refs
Brown rice, barley, mixed grains, corn, wheat and wheat flour	South Korea	1.5–4.1[a]	[59]
Brown rice	South Korea	12.4–41.2[a]	[45]
Component feed, chicken feed, pig feed, cattle feed	South Korea	1.6–16.7[b]	[45]
Corn	South Korea	15.3–207.4[a]	[45]
Mixed grains	South Korea	11.5–30.4[a]	[45]
Raw materials such as corn, soybean meal, peanut products, cassava, rice bran, broken rice and fish meal and complete animal feeds	Thailand	0–25[c]	[16]
Rice, glutinous rice, brown rice, corn dry, breakfast cereals, barley, wheat, wheat flour, mixed grains	South Korea	22.2–37.2[b]	[45]
Tea corn, rice, barley, black bean, wheat, wheat powder	South Korea	54.8[b,d]/35.2–431[b,e]	[45]
Wheat, wheat flour, barley	South Korea	0[a]	[45]

[a] Analyzed with HPLC-FLD (High Performance Liquid Chromatography with Fluorescence detection).
[b] Analytical method not mentioned.
[c] Analyzed with enzyme-linked immunosorbent assay.
[d] Occurrence survey in year 2009 compared to occurrence survey in year 2011.
[e] Occurrence survey in year 2011.

foodstuffs, as well as to ensure fair practices in the food trade. Various factors play roles in decision-making processes focused on setting limits for mycotoxins including the availability of toxicological data of mycotoxins, the availability of exposure data of mycotoxins, knowledge of the distribution of mycotoxins concentrations in commodity or product lots, the availability of analytical methods, legislation in other countries where the exposure rate exists, and the need for sufficient food supply [60]. The regulatory philosophy may also vary in different areas of the world. In developing countries, the adequate level of protection must take into consideration the amount of food available. If food supplies are already limited, drastic legal measures may cause food shortages and excessive consequences. Thus, there is a wide range of varying standards among different national or multilateral agencies [61].

Countries have the legitimate right to protect their consumers from the toxic effects of these mycotoxins. However, setting mycotoxin regulations is a complex and difficult activity that involves many factors and interested parties. The first limit for mycotoxins was set in the late 1960s for aflatoxins. Until the late 1990s, setting of mycotoxin regulations was mostly a national affair. Up to 2003, approximately 100 countries have developed specific limits for mycotoxins in foodstuffs and feedstuffs. It represented an increase of approximately 30% compared to 1995 [1]. As aflatoxins are regulated most strictly and worldwide, all countries with mycotoxin regulations in Asia have at least regulatory limits for aflatoxin B1 or total aflatoxin (the sum of aflatoxins B1, B2, G1, and G2) in food, followed by aflatoxin M1, patulin, ochratoxin, deoxynivalenol, and zearalenone [1]. Although each country has its own specific regulations for mycotoxins, harmonized regulations have yet to be established. Association of Southeast Asian Nations (ASEAN) Reference Testing Laboratories (ARLs) have been established for mycotoxins as well as pesticide residues, veterinary drugs, microbiology, heavy metals, and genetically modified organisms. Six laboratories, located in Malaysia, Singapore, Thailand, and Vietnam, have been selected to serve as ARLs to develop the network of ARLs, then further to develop National Reference Laboratories [62]. In addition, other documents such as the ASEAN Common Food Control Requirements, the ASEAN Common Principles for Food Control Systems, the ASEAN common Principles and Requirements for the Labeling of Prepackaged Food, and the ASEAN Common Principles and Requirements for Food Hygiene have been finalized and will serve as guiding principles for setting up regulations of mycotoxins in food in Asian countries [61].

In the international seminar on risk assessment and risk management of mycotoxins for food safety in Asia, representatives from several countries including Indonesia, Japan, Philippine, and Thailand shared information on the regulation situation and management of mycotoxins in their own countries, the details of which are briefly summarized in the following sections.

3.1. *Indonesia*

Indonesia, a tropical country with relatively high humidity and temperature, is currently struggling with aflatoxin-contaminated peanuts. Peanut, which is mostly cultivated by small farmers, is the commodity found with the highest contamination of aflatoxins and other mycotoxins in Indonesia [63]. This problem is hardly known by stakeholders in food and feed business, such as farmers, traders, and small food processing industries. There was a need therefore to enhance knowledge about these toxins to improve awareness in the food safety aspect, in order to avoid or reduce their occurrence in food or feed, as well as to publicize the regulations, set up priorities, and establish integrated programs and activities to support the government and other stakeholders [64]. Indonesia has adopted regulations on mycotoxin contamination maximum level as part of its harmonization efforts with the world trade society. The Indonesian Food and Drug Control Agency established the following maximum contamination levels of total aflatoxin: 50 ppb for feed (corn; 1995), 35 ppb for total aflatoxin in food, and 20 ppb for AFB1 (2004). The Indonesian National Standardization Agency in

1995 launched SNI 7385-2009 (Indonesian National Standard), and standard levels of mycotoxins currently of concern are aflatoxins (B1, B2, G1, G2, M1, and M2), deoxynivalenol, fumonisins B1 and B2, ochratoxin, and patulin in specific foods. However, aflatoxin levels found in peanut as well as in some peanut products are much higher than the regulatory limit [65].

In Indonesia, research ventures on aflatoxins have been conducted by the faculty of the Agricultural Technology Gadjah Mada University, where the Center of Excellence in Mycotoxin Studies has been set up since 2010. The Faculty of Agriculture Technology, Gadjah Mada University, along with related government agencies, research institutes, universities, industries, farmers' groups, and communities have set up an Aflatoxin Communication Forum, which conducts a meeting annually [64]. According to the surveillance data of aflatoxin occurrence on corn and peanut, improper storage condition or improper drying at farmers' site mainly cause further growth of the mold during storage of high-moisture crops. During this time, the kernel of corn or peanut still has a high moisture content and is thus susceptible to fungal attack. Corn or peanut should be dried as soon as they are harvested [63,64]. Because of the awareness of these problems, the peanut-based food industries in Indonesia have been requested to attend the training for good agricultural practices with emphasis on the selection of seeds resistant to insect and drought, ways of harvesting to ease drying, and postharvest handling in order to reduce mold attack and subsequent toxin contamination. Through an integrated management effort, it is believed that aflatoxin contamination in agricultural commodities can be controlled, and the regulation can be reinforced in a proper way and in a timely manner [64].

3.2. *Japan*

Japan has a mild climate. Under this condition, some mycotoxins including patulin, ochratoxin, and fumonisin can occur in agricultural products; this condition, however, is not suitable for the production of aflatoxins [66]. Nevertheless, contaminated aflatoxins have been reported in some commercial foods, mainly in peanut, pistachio nut, buckwheat, corn, coix seed, barley, and wheat, which are imported from other countries. To ensure consumer safety, regulatory limits have been set for AFB1 at 10 μg/kg in all foods, patulin at 50 μg/kg for apple juice, and a tentative guideline level for DON at 1.1 mg/kg for wheat and other products [66].

The Food Safety Commission (FSC) was established on July 1, 2003, as a part of the Japanese Cabinet Office, based on its founding regulation of Food Safety Basic Act (Law No. 48, May 23, 2003/12/15). The top priority of the FSC is to take all actions under the basic understanding that the protection of the Japanese general public is the paramount consideration. The FSC is primarily composed of seven commissioners. As its subordinate structure, the FSC has 14 Expert Subcommittees, among which the risk assessment of mycotoxins is carried out at the Expert Subcommittee of Natural Mycotoxins [67]. The establishment of the FSC was really a turning point for the safety evaluation against mycotoxin risks in Japan, in accordance with the 56th Joint FAO/WHO Expert Committee on Food Additives (JEFCA) meeting (2001), which evaluated the risks of several important mycotoxins such as fumonisin, ochratoxin, DON, and T-2. Thereafter, the situation of mycotoxin research and management in Japan has changed dramatically. Systematic and comprehensive projects on the method validation of mycotoxin analyses and surveillances for several mycotoxins have been successfully organized under the Ministry of Health, Labor, and Welfare. The results obtained from these projects have been practically implemented for the risk assessment of mycotoxins at FSC [68].

The Japanese Society of Mycotoxicology, formerly known as the Japanese Association of Mycotoxicology, was founded in 1974 as an academic organization with the objective of contributing to scientific, technological, and industrial developments in order to enhance scientific knowledge concerning toxicology, biology, and chemistry related to mycotoxins and mycotoxin-producing fungi, through membership networking, annual meetings, international symposia, seminars, and publications [69]. The organization consists of researchers and technologists from national and local government institutes, universities, private institutes, and university students in various fields. At the moment, the society has about 200 regular members and 50 maintenance members from the private sector [69]. The society holds scientific meetings twice a year. Technical seminars and workshops, focusing on such topics as mycotoxin analysis and fungi identification, have been organized. The society publishes the journal *Mycotoxins* twice a year (comprising one volume). In order to promote the circulation of scientific and technological information that has been accepted after peer reviews and published, all past issues of the journal are provided in J-STAGE (Japan Science and Technology Information Aggregator, Electronic) [68,69]. To promote its international activities further, the society has organized the International Symposium of Mycotoxicology. The society has also cosponsored several international symposia including the Third International Mycology Conference in 1983 (Tokyo), and the International Union of Microbiological Societies 2011 Congress in 2011 (Sapporo) [68]. Recently, the society has promoted an exchange of ideas among researchers and government officers from various Asian countries. Moreover, in order to solve the problems on insufficient inspection techniques that have caused trade stagnation of agricultural produce especially those originating from developing countries, the Japan International Cooperation Agency launched a program for mycotoxin education in food safety. This program provides general knowledge, analytical techniques, and mycotoxin precautions for 3 months consisting of lectures, laboratory practices, and observations, with the aim of consolidating pre-export food examination system and enabling participants to learn the proper methodology and technology for handling mycotoxins in food [68].

3.3. *The Philippines*

In the Philippines, a technical working group has been formed that is responsible for the update and establishment of the safety level of aflatoxins in corn for the Philippine National Standard through gathering of relevant data from major corn-producing areas in the country, including information from scientific institutes within Metro Manila. Data gathering includes—but is not limited to—survey, laboratory analysis, and research [70].

The risk assessment program examines the public health risk associated with the consumption of corn containing aflatoxin based on the results of food analytical surveys obtained from the different regions in the Philippines and the toxicological evaluation of the health impact undertaken by the JEFCA in 2001 [70]. Furthermore, it will serve as the basis for the establishment of maximum levels of aflatoxin in corn. The study is ongoing, collecting information for the risk assessment of aflatoxin in corn [70].

3.4. *Thailand*

In Thailand, careful control of mycotoxins has been administered and financially supported by the Thai government through ministries and several institutes. The National Committee on mycotoxin control in agricultural commodities in Thailand has been set up, composed of members from both the private and public sectors, which cover the areas of research and development, extension, and marketing [71]. The government agencies involved in this program include the Cooperatives Promotion Department, Office of Agricultural Economics, Department of Agriculture, Department of Agriculture Extension, Department of Foreign Trade, Board of Trade of Thailand, Bank of Agriculture, and Agricultural Cooperatives and the National Economic and Social Development Board. This committee is tasked to: (1) publicize the nature and importance of mycotoxin especially for export products; (2) devise and evaluate the effective mycotoxin control measures applicable to each stage in food supply chain; (3) coordinate mycotoxin research and maximize collaborative studies to increase efficiency and reduce excessive duplication of projects; and (4) regularly monitor the mycotoxin contents of products intended for exporting, so that any problems can be recognized early and remedial actions can be taken promptly [71]. Much of the mycotoxin research in Thailand can now be properly coordinated, thanks to the influence of the national committee. Assistance from other countries to provide funding, training, and staff is still needed; such support has played a significant role in mycotoxin control in the past. Various foreign agencies have given support to the Department of Agriculture through bilateral or multilateral assistance.

During the international seminar on risk assessment and risk management of mycotoxins for food safety in Asia, a meeting was also held for the Thai committee. All committee members agreed to establish the Mycotoxin Association of Thailand, whose aims are as follows: (1) to enhance scientific knowledge concerning any disciplines related to mycotoxins and toxigenic fungi; (2) to promote the interests and elevate the standards of mycotoxin in food and feed; and (3) to promote communications that enhance understanding among the members of the association by sharing of scientific and other relevant information. The committee members strongly believe that the association will promote research on mycotoxins, leading to prevention and reduction in exposure to mycotoxins, and thus enhance food safety and promote public awareness of mycotoxin through education, advocacy, and research efforts.

4. Conclusions and recommendations

Although mycotoxin contamination in food and foodstuffs in Asia have been updated in the past 10 years, relevant information remains insufficient, which makes it difficult to assess the exposure of Asian populations to mycotoxins. The risk of contamination by mycotoxins is an important issue of food safety and quality control of foods and feeds. Avoiding mycotoxin occurrence in the food chain is a primary goal that requires understanding of the sources and routes of contamination. Regarding the inspection and analysis of mycotoxins in foods and feeds, there is a clear and urgent need to develop methods that are more rapid, precise, sensitive, selective, and inexpensive. Collaborations and cooperative research efforts among scientists and laboratories in Asian countries should be encouraged to assess the extent of human exposure to mycotoxins in this region. Regarding the regulatory aspect, the establishment of government-authorized regulatory guidelines and laws is essential. Continuing support from national governments or regional communities to encourage and fund activities that contribute to reliable exposure risk assessment and risk management of mycotoxins in their respective regions is also important to protect consumers from the health threat posed by mycotoxin contamination.

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