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REVIEW

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A call for aflatoxin control in Asia

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Abstract

Aflatoxins are secondary metabolites, produced by some fungal species of the genus *Aspergillus*, posing health and economic implications throughout the world. Developing countries in Asia usually have tropical conditions and grow crops susceptible to aflatoxin proliferation. Aflatoxin proliferation is more frequent in tropical regions due to optimal climate conditions required for their production. In general, the developing countries in Asia lack control and regulation strategies, like poor harvesting practices, improper storage and poor transportation conditions resulting in major losses from farm to fork level. A number of aflatoxin positive cases above safe limits have been reported in Asia in various commodities being consumed by the local population. This not only exposes to health issues like growth impairment, immunosuppression, hepatic disorders etc. but also result in heavy economic losses due to trade restrictions. However, rigorous aflatoxin standards mean that many nations would export their best quality food and keep contaminated food domestically, resulting in higher aflatoxin exposure in low or middle-income nations, where hepatitis prevalence is high. Aflatoxin control is needed to protect the Asian population from the risks of aflatoxins and to ensure good quality safe availability of commodities throughout the world by trade. In recent years a number of bioproducts have been introduced successfully worldwide that are safe, efficient and ecofriendly. Such initiatives may be taken in Asia as well to protect our food and feed commodities from aflatoxin contamination.

Keywords Aflatoxins, Asia, Health risks, Trade restrictions, Biological control

Background

The world's human population has raised to approximately 8 billion heads, alarming with the prime threat to food security and safety, subsequently resulting in hunger and starvation of more than 700 million people daily with constraining access to cereals, grains and other staple foods (FAO Global Quarterly Report 2021). The production of crops is not increasing proportionally to human population in the world, which is further deteriorated by natural disasters and plant pests and diseases. The majority of spoilage in the food and feed crops throughout the world is caused by fungi, and up to 60–80% of the total world's food crops are damaged by mycotoxins, with aflatoxins as the prime etiological agent (Eskola et al. 2020). Aflatoxins not only damage the food crop but also pose serious threats to animal and human health when consumed.

Aflatoxins are secondary metabolites fluorescent heterocyclic compounds, produced by fungi- *Aspergillus* spp., in particular *Aspergillus flavus* and *A. parasiticus* (Gourama and Bullerman 1995; D'Mello 2003). Of the more than 18 different forms and metabolites currently recognized, four major types of aflatoxin are the best known and studied: aflatoxin B1 (AFB1), aflatoxin B2 (AFB2), aflatoxin G1 (AFG1) and aflatoxin G2 (AFG2) (Goldbalt 2012). Diets with high levels of these contaminants for longer periods can cause: stunted growth, immunosuppression, impaired food conversion, liver cancer and sometimes may even prove to be fatal (Coursaget et al. 1993; Gieseker 2004; Gong et al. 2008; Leroy et al. 2018; Voth-Gaeddert et al. 2018). Aflatoxin contamination of crops results in high risk of health hazards, therefore in order to prevent this, regulations are being

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developed world-wide. However, developing countries usually fail to implement these regulations, resulting in reduced trade and food insecurity (Matumba et al. 2017a, b; Chilaka et al. 2022).

For the past decade studies revealed 55% of the cereal grains worldwide were found to be contaminated by aflatoxins (Lee and Riyu 2017). Aflatoxin contamination of peanuts, particularly AFB1, AFB2, AFG1 and AFG2 has also peaked to an alarming situation, which in turn results in production of contaminated peanut products like peanut butter, granola bars etc. which are sold in the markets of developing countries of Asia and Africa (Jiang et al. 2005; Waliyar et al. 2003).

Aflatoxin- a silent killer

Aflatoxins go often undetected, despite their great negative impact. As aflatoxins are odorless, colorless and tasteless, consumers are unable to detect aflatoxins and they cause harms to the health of population (Cassel et al. 2001; Udomkun et al. 2017). Consuming aflatoxin contaminated food directly, or the animal products, previously on aflatoxin contaminated feed, may result in immune suppression, growth retardation and even, death (Gieseker 2004; Probst et al. 2010; Kamala et al. 2018).

International Agency for Research on Cancer (IARC) has declared group-1 aflatoxins (comprising AFB1, AFB2, AFG1, AFG2, AFM1) to be highly carcinogenic to human health (IARC 2002). Exposure to aflatoxins can indeed cause detrimental health effects. These mycotoxins act as potential pathogens, mutagens, teratogens and genotoxic complexes, which means they have the ability to cause acute and chronic health effects, including carcinogenicity (Peles 2019; Jalili and Scotter 2015). The exposure to aflatoxin contaminated food may increase the risk of incidence of hepatocellular carcinoma up to 30 times, especially in case of exposure to hepatitis B virus (El-Serag 2020; Bruix et al. 2016; Yoshida et al. 2016). Aflatoxins can pass the blood-testis barrier and cause damage to the testicular tissue, negatively affect spermatogenesis, and result in the deterioration of sperm parameters (Ataman 2014). Even the inhalation of air particles contaminated with aflatoxins may result in tumorous growths in respiratory system (Agag 2004).

Lactating mothers who consume aflatoxin-contaminated food, produce milk that may be hazardous for the breast-feeding infants (Radonić et al. 2017). The AFB1 present in the food is converted to AFM1, that may instigate immunosuppression, retarded growth, hepatic disorders and carcinogenic effects in children (Khlangwiset et al. 2011).

Aflatoxins are not only harmful to human health but also implicate a detrimental effect on the health of animals. In developing countries, 40% of the loss in animal production has been recorded due to aflatoxin contaminations and results in either acute or chronic illness (Wagacha et al. 2008). Both directly affect the economy of the farmers, either by reducing the production of the animal or by causing health impairment to the animal.

Aflatoxins may cause morbidity as well as mortality in animals, which has been observed in various cases in history. The deaths of 100,000 turkeys in England in the 1960's set up an alarming situation, when it was noted that they were fed upon feed imported from Brazil (Homei and Worboys 2013). Since then, various cases of deaths of animals like rainbow trout, pigs, dogs, cattle have been observed in different parts of the world due to ingestion of aflatoxin contaminated feed (Council of Agriculture Science and Technology 2003). Aflatoxins have negative impacts on the health and production of human as well as animals (Unnevehr and Grace 2013) as major outbreaks have occurred in the history that have affected both animal and human populations, as described in Fig. 1.

In a nut shell, it is inferred that aflatoxin contamination has a negative effect on well-being of humans and animals, revenue, food security and trade (Wu 2015; Bandyopadhyay et al. 2016).

Aflatoxins—a threat to Asia

Up to 70% of the world inhabitants are exposed to aflatoxins beyond safe limits (Brown 2018). The most common staple food throughout the world are cereals and cereal by-products, out of which maize and rice are most prone to aflatoxin contamination due to the modified agricultural practices (Temba et al. 2017; Hesseltine 1974). Approximately, more than 4.5 billion people living in developing countries of Africa and Asia are exposed to unsafe aflatoxin levels due to contaminated food consumption (Williams et al. 2004). About 300 million people in South Asia live in poverty, 70% belong to the rural population. Figure 2 represents a map showing wide distribution of Aspergillus in Asia.

South Asia

Annually, almost 200 billion children worldwide face impaired growth and development with a significant prevalence in South Asia. These children endure deprived health conditions leading to financial burden on affected nations (Black et al. 2013; Stevens et al. 2015).

India has faced a number of serious aflatoxin outbreaks, causing harms to human and animal lives as well as, substantial financial losses to the country. An aflatoxin outbreak faced by India for two consecutive months in 1974 resulted in the death of 200 lives. The reason was diagnosed as high aflatoxin content in maize used as a staple food, resulting in local population suffering from acute

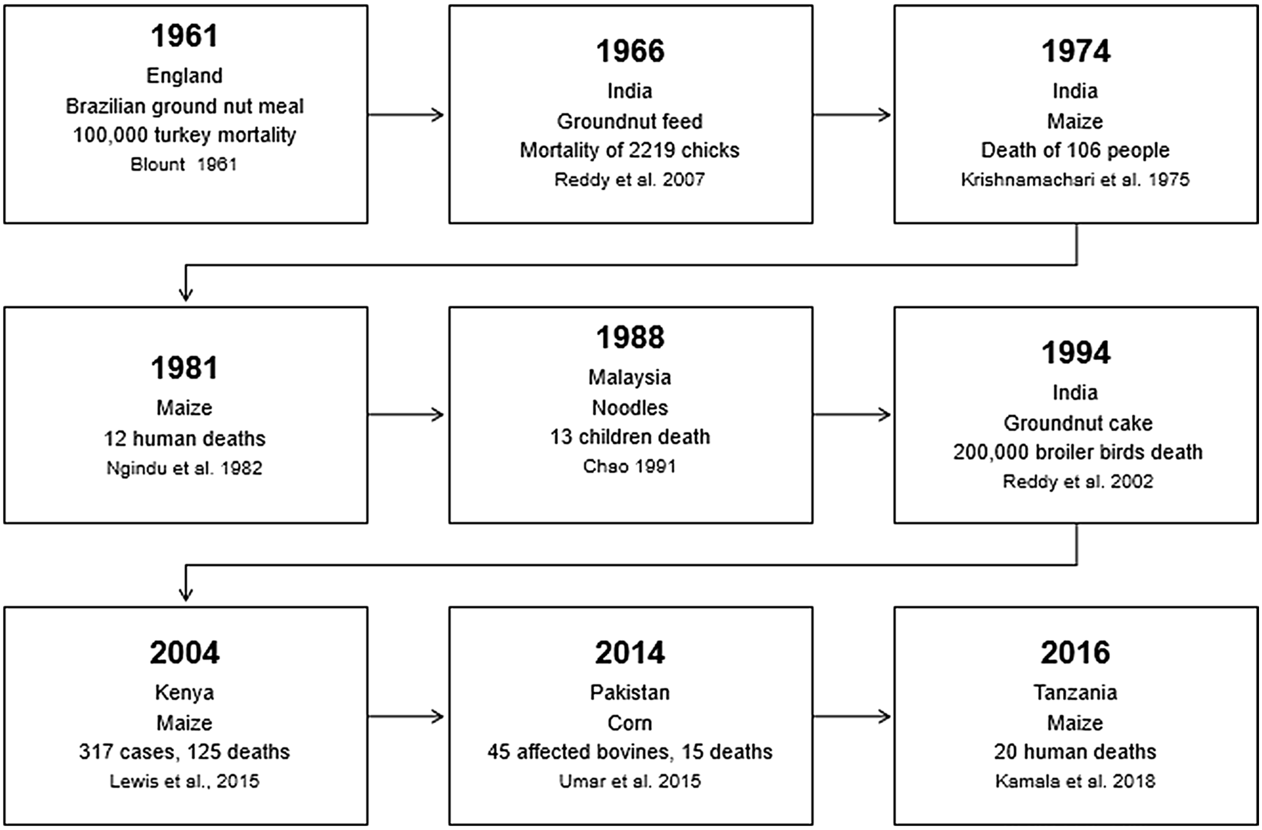

Fig. 1 Major aflatoxin outbreaks reported in animals and humans

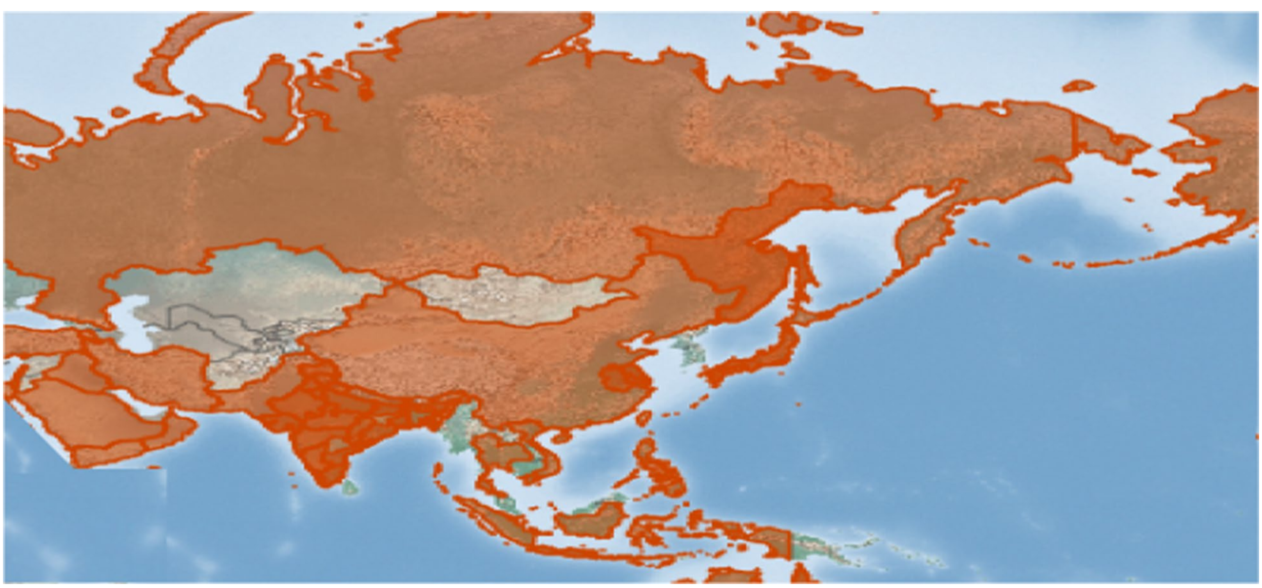

Fig. 2 Regional distribution of *Aspergillus* in Asia (CABI Compendia, 2023)

hepatitis (Krishnamachari et al. 1975). In 1982, another outbreak of aflatoxicosis occurred in poultry in Andhra Pradesh, India resulting in complete and devastating mortality rate reaching 100% (Choudary and Rao 1982). Since then, a number of outbreaks, as well as, case studies have become prominent to emphasize the importance of taking control measures for eliminating aflatoxins, as mentioned in Table 1.

Efforts are being made by governmental agencies, such as Agricultural and Processed Food Products Export Development Authority (APEDA) and the Food Safety and Standards Authority of India (FSSAI), have developed and implemented analytical methods and quality control procedures to monitor mycotoxin levels in a range of food matrices and assess risks to human health over the last two decades (Chatterjee et al. 2023).

Mycotoxin contamination in agricultural products also continues to be a problem for Pakistan to export its commodities. The location of Pakistan, is such that it gives mycotoxins a favourable hot and humid environment to proliferate on crops (Majeed et al. 2013). AFM1 poses a serious threat to the dairy industry, as it is present in milk and dairy products throughout the world. It is common in developing countries, like India, Bangladesh, Iran, Pakistan and others, to have frequent occurrence of aflatoxins in food commodities above safe limits (Sharma et al. 2020; Sumon et al. 2021; Fallah et al. 2011; Iqbal et al. 2013a, b).

Currently, there are no regulations of AFM1 in milk and milk products in Pakistan. The concept of "aflatoxins" remains largely unfamiliar to almost 95% of the farmers in Pakistan (Yunus et al. 2022). In 2010, a study

Table 1 Studies with aflatoxin positive cases in South Asian Countries

S. no	Area	Country	Commodity	Aflatoxin Type	% Positive samples	Reference
1	20 states	India	Rice	AFB1	2%	Reddy et al. 2009
2	Haryana	India	Milk	AFM1	21%	Sharma et al. 2020
3	Lucknow	India	Infantile milk products and liquid milk	AFM1	99%	Rastogi et al. 2004
4	11 states	India	Maize	AFB1	26%	Bhat et al. 1997
5	Various regions	India	Wheat grain	AFB1	16%	Toteja et al. 2006
6	Punjab	India	Stored and damaged rice	AFB1	85.7%	Siruguri et al. 2012
7	Lahore and Multan	Pakistan	Processed milk and tea whiteners	AFM1	56%	Ahmad et al. 2019
			Milk samples		66%	
8	Punjab	Pakistan	Sweets (mithai)	AFM1	97%	Sadia et al. 2012
9	Karachi	Pakistan	Chili	AFB1	66%	Shamsuddin et al. 1995
10	Lahore and Faisalabad	Pakistan	Processed food	AFB1, AFB2	38%	Mushtaq et al. 2012
11	Punjab	Pakistan	Raw peanut with shell	All	59%	Iqbal et al. 2013a, b
			Raw peanut without shell		55%	
			Roasted peanut without shell		68%	
			Peanut butter		50%	
			Peanut cookies		42%	
			Peanut nimko		20%	
12	Punjab	Pakistan	Paddy rice	All	64%,	Iqbal et al. 2012
			Parboiled		38%	
			Brown		33%	
			White		42%	
			Broken		50%	
13	Punjab	Pakistan	Chilies	AFG2 and AFB2	33%	Iqbal et al. 2011
14	Dinajpur	Bangladesh	Fresh maize	AFB1 and AFB2	28%	Rafik 2020
			Stored maize		10%	
15	Dhaka	Bangladesh	Raw, UHT and pasteurized milk	AFM1	25%	Sumon et al. 2021
16	Dhaka, Rajshahi, Chittagong, Sylhet, Khulna and Barisa	Bangladesh	Maize	All	37%	Bhuyian et al. 2013
17	Kathmandu valley	Nepal	Maize	AFB1	42.5%	Pokhrel et al. 2005
18	Various regions	Nepal	Maize and maize products	AFB1	20%	Koirala et al. 2005
19	Selected clusters	Nepal	Maize	AFB1	15.7%	Rai et al. 2013
20	Seven provinces	Sri Lanka	Milk	AFM1	9.2%	Pathirana 2010
21	Various regions	Sri Lanka	Dry chili	AFB1	67%	Yogendrarajah et al. 2014

revealed 81% of AFM1 detection in raw milk collected from Lahore, the second most populous city of Pakistan, which depicts an alarming condition of aflatoxin exposure in the country (Muhammad et al. 2010).

Aflatoxin contamination of spices has also been detected in samples from various countries such as, Pakistan, Malaysia, Iran, India, Turkey, Spain etc. (Reddy et al. 2001; Aydin et al. 2007; Paterson 2007; Santos et al. 2010; Iqbal et al. 2010; Jalili et al. 2012). Pakistan is also the sixth largest exporter of red chilies, contributing to 1.5% of the share in total gross domestic product (GDP), yet aflatoxin contaminations at high levels are reported in red chilies grown in Pakistan (Hussain and Abid 2011). Controlling aflatoxin contamination may enhance chili export to even a better level. According to a study, some chili samples had aflatoxin contamination eight times more than the permissible limits set by the European Union (Iqbal et al. 2011). Although new improves methods are being introduced in cultivation and production but farmers in Asia use traditional methods for storage of crops that elevate the risks of aflatoxin contamination in crops. Due to high aflatoxin contamination affecting crops in Pakistan and very few testing laboratories, the local community is exposed to carcinogenic risk. In a study, branded and non-branded corn samples were tested, where AFB1, AFB2 and AFG1 were found to be several times higher than the prescribed limits by EU (Hussain et al. 2020).

Stunted growth is highly prevalent in Nepal, and one of the suspected causes is aflatoxin exposure (Nepali et al. 2019). A trial was conducted in Nepal to confirm the co-relation between chronic exposure of aflatoxin content with body growth. The four-year study confirmed that long term low exposure to pregnant mothers and infants caused impaired long-bone development in children, increasing the chance of stunted growth (Andrews et al. 2021).

In Sri Lanka, almost 30% of the imported coconut oil samples were found to be contaminated with aflatoxins, which is alarming for the industry (Karunarathna 2019). The suspected cause of this contamination was poor agricultural practices by the farmers and inadequater testing facilities. Regulations need to be implemented locally to meet the international requirements to export agricultural commodities and improving revenue generated from trade and for provision of healthy, contamination free commodities to local population (Yogendrarajah et al. 2014).

Corn is a major staple food in Sri Lanka, which is prone to AFB1 contamination. A study was conducted in Anuradhapura, Sri Lanka, to determine the aflatoxin contents in corn and corn-growing soils. It showed the aflatoxin content in corn increased with high aflatoxin content of soil used for corn cultivation. The study showed aflatoxin content to be higher in the soil in which the corn was grown, rather than the corn kernels themselves. By implementing control measures to reduce aflatoxin content in the soil, the presence of aflatoxins to the maize kernels can be effectively controlled. This in turn will lead to a reduced mycotoxin exposure to the local population (Jayaratne 2020). Table 1 illustrates several studies showing occurrence of aflatoxins in various commodities in South Asian countries.

East Asia

In China, aflatoxin contamination in rice was reported about 50% (Ali 2019). A research on peanut butter and sesame paste showed AFB1 presence above EU permissible limits. These results were positive for 37% of peanut butter samples and 32% of sesame paste (Li et al. 2009).

Various studies in Japan concluded that the presence of aflatoxins in various commodities is within the permissible safe limits. A survey illustrated that the total dietary intake of common Korean man exceeded the safe limits, and rice stands to be the major culprit for the bearing high aflatoxin content (Park et al. 2004).

To assess the safe consumption of food items, a research was conducted to evaluate aflatoxin content in peanuts and peanut products available in Taiwan. These commodities were imported from China, Indonesia, Thailand, United States and Philippines, which exceeded the safe limits set up by regulatory authorities (Lien et al. 2019).

Herbal drugs from various regions of South Korea were tested for AFB1 presence, resulting 59% positive cases above safe levels (Shim et al. 2012).

Table 2 presents the occurrence of aflatoxins in food samples across East Asia.

South East Asia

In 1991, the total social cost per year due to aflatoxin contamination of maize in Thailand, Indonesia and Philippines was estimated to be around 319 million $AUS (Balendres et al. 2019). In 2009, a burden of US$ 6.9 million per year has been estimated to exist (Lubulwa et al. 2015). These studies available might be outdated, potentially depicting lower levels of aflatoxins in the past and it is plausible that levels have potentially increased since then.

Thailand was one of the top exporting maize country in 1980's but its export potential has reduced due to a number of reasons; one of which is aflatoxin contamination, especially during rainy years (Ekasingh et al. 2001).

In 2020, a study was conducted in Malaysia to determine aflatoxin content in corn. The results showed that

Table 2 Studies with aflatoxin occurrences in food and feed samples in East Asia

S.no	Area	Country	Commodity	Aflatoxin Type	% Positive Samples	References
1	Zhuqing village	China	Ground corn	AFB1	76.7%	Wang et al. 2001
			Cooking peanut oil		66.7%	
			Rice		23.3%	
2	Central China	China	UHT milk	AFM	1.8%	Xiong et al. 2018
			Pasteurized milk		59.5%	
			Dairy cow feedstuff	AFB1	6.3%	
3	Various regions	China	Spices	AFB1	11%	Zhao et al. 2013
4	Various regions	China	UHT milk	AFM1	20.3%	Zheng et al. 2013
			Pasteurized milk		65.4%	
5	Different regions	China	Pig feed	AFB1	1.5%	Zhao et al. 2021
			Poultry feed		1.2%	
			Ruminant feed		12.8%	
6	Various regions	South Korea	Herbal drugs	AFB1	59%	Shim et al. 2012

45% of the samples contained aflatoxins, in which the highest prevalence was in the region Kampong Raja (Rahim Khan et al. 2020).

In a study conducted in Indonesia, 30.6% of broiler feed samples used at small-scale farms had aflatoxin content more than the allowed limit set by standard setting bodies (Thaha et al. 2021).

Middle East

Significant loss in Yemen's poultry industry have been reported due to aflatoxin contaminated feed. Aflatoxin contamination in post-harvest crops is already high, which further increases in storage conditions (Algabr et al. 2018).

The content of aflatoxin does not denature on boiling, pasteurizing or treating with Ultra-high Temperature (UHT) (Prandini et al. 2009). Iranian milk products were tested in 2011 for AFM1 content, which exceeded the standards set by the Institute of Standards & Industrial Research of Iran (ISIRI) and EU (Fallah et al. 2011).

AFM1 content is only found in milk and milk products and are not found in animal's feed source. It can enter the animal's body through animal feed which contains AFB1 and are then converted to AFM1 in the animal's body and are later released in milk and urine produced (Veldman et al. 1992). A study in Qatar showed incidence of AFM1 in dairy products, when tested for confirmation of aflatoxin contents. The samples of milk, yoghurt, cheese, butter and laban showed 85%, 76%, 85%, 67% and 76% aflatoxin content respectively, although the content of AFB1 did not exceed the safe limits (Hassan et al. 2018).

A study was conducted on yoghurt samples obtained from five different countries of Asia to determine aflatoxin contents. About 31.25% of the samples from Turkey and 32.35% Lebanon contained AFM1 exceeding the safety standards set by the EU (Mohammadi et al. 2021).

Impact on socio-economics of Countries

Aflatoxins pose a global threat, yet the major impacts in the developing countries, specifically due to their geographic location that provides favourable factors for aflatoxins to proliferate and also due to poor regulatory implementations. The highest incidence of aflatoxins has been detected in the products of Sub Saharan African countries, like Kenya, Gambia, Tanzania etc. and Asian countries like Pakistan, India, China, Thailand, Vietnam etc. which eventually increases the risk of outbreaks and incidence of hepatocellular carcinomas in the local population (Liu and Wu 2010).

In developing countries of Africa and Asia, more than 5 billion human population is potentially exposed to contaminated products with aflatoxin contents more than the permissible limit due to poor safety checks and regulations (Williams et al. 2004). Due to absence of proper testing of aflatoxin levels, aflatoxin contaminated commodities enter into the food and feed supply chains increasing the input costs, that either get rejected by international markets or are consumed by the local population, posing a silent threat (Bhat et al. 2010; Chang et al. 2002).

Due to health problems caused by aflatoxins, the developed nations have imposed rigorous regulations for the controlled movement of food commodities from other countries, as well as their own local produce (Benkerroum 2020).

The biggest constraint arises at the regulatory levels between developed and developing nations. The developed countries have rigorous rules and regulations to protect their human and animal populations from aflatoxin exposure through food and feed commodities checkingscreening local and imported products. However, developing countries that are producing a number of commodities either fail to make proper regulations or implement them. This situation causes problems to both, as the exporting country fails to generate their agricultural revenue and the importing country fails to meet their local demands due to unavailability of aflatoxin safe food (Okoth et al. 2018; Gilbert et al. 2018; Van Egmond and Jonker 2004). This problem does not only affect the financial revenues of farmers but also the operators, processors and exporters of the region (Williams 2008; Wu 2015).

Regulatory authorities

Developed countries have rigorous regulations for the control of aflatoxins and their implementation will not only ensure safety of human population and animal population of the nation but will also improve economy (Cheli et al. 2014; Matumba et al. 2017a, b; Chilaka et al. 2022) (Tables 3, 4). Many Asian countries have developed regulatory bodies that check and maintain aflatoxin levels within the countries, as represented in Fig. 3.

The EU, FDA (Food and Drug Authority), FAO (Food and Agriculture Organization) have set safety limits of aflatoxin content in food and feed stuffs as indicated in Table 5. These safety limits are also applied onimported goods from producing countries (Van Egmond and Jonker 2004; FDA 2021).

Table 3 Studies with aflatoxin occurrences in food and feed samples in South East Asia

S.no	Area	Country	Commodity	Aflatoxin Type	% Positive Samples	References
1	Kampong Raja, Rose Valley, Kea, and Klebang farms	Malaysia	Corn	All	45%	Rahim Khan et al. 2020
2	Various super markets	Malaysia	Raw peanut kernels	All	10.71%	Arzandeh et al. 2010
3	Penang	Malaysia	Nuts and nut products	AFB1	13.3%	Leong et al. 2011
4	Sidenreng Rappang Regency	Indonesia	Broiler feed samples	All	30.6%	Thaha et al. 2021
5	Province of Yogyakarta	Indonesia	Milk	AFM1	30.1%	Nuryono et al. 2009
6	Jambi, Lampung, Pontianak and Surabaya	Indonesia	Indonesian palm kernel cake and copra meal	All	50%	Rieter et al. 2013
7	Various regions	Malaysia and Philippines	Corn products	All	100%	Ali et al. 1999
			Peanuts		65%	

Table 4 Studies with aflatoxin occurrences in food and feed samples in middle east

S.no	Area	Country	Commodity	Aflatoxin Type	% Postive Samples	References
1	Different regions	Yemen	Powdered milk	AFM1	66.66%	Murshed, 2020
			Liquid milk		68.42%	
			Yoghurt		87.09%	
			Cheese samples		81.39%	
2	Different areas	Yemen	Cheese	AFM1	32.6%	Murshed, 2022
3	Sana city	Yemen	Green coffee beans	All	84%	Humaid et al. 2019
			Roasted coffee beans		62%	
4	Tehran, Esfahan, Tabriz and Shiraz	Iran	Cow dairy products	AFM1	35.2%	Fallah et al. 2011
			Goat milk products		10.8%	
			Sheep milk products		25%	
5	West-Azerbaijan	Iran	UHT (Ultra high temperature treated) milk	AFM1	54.2%	Tajik et al. 2016
6	Kerman and Rafsanjan	Iran	Pistachio nuts	AFB1	11.8%	Cheraghali et al. 2007
7	Kermanshah and Mazandaran provinces	Iran	Maize	AFB1	15.68%	Ghiasian et al. 2011
8	-	Qatar	Imported commodities	All	14%	Abdul kadar et al. 2002

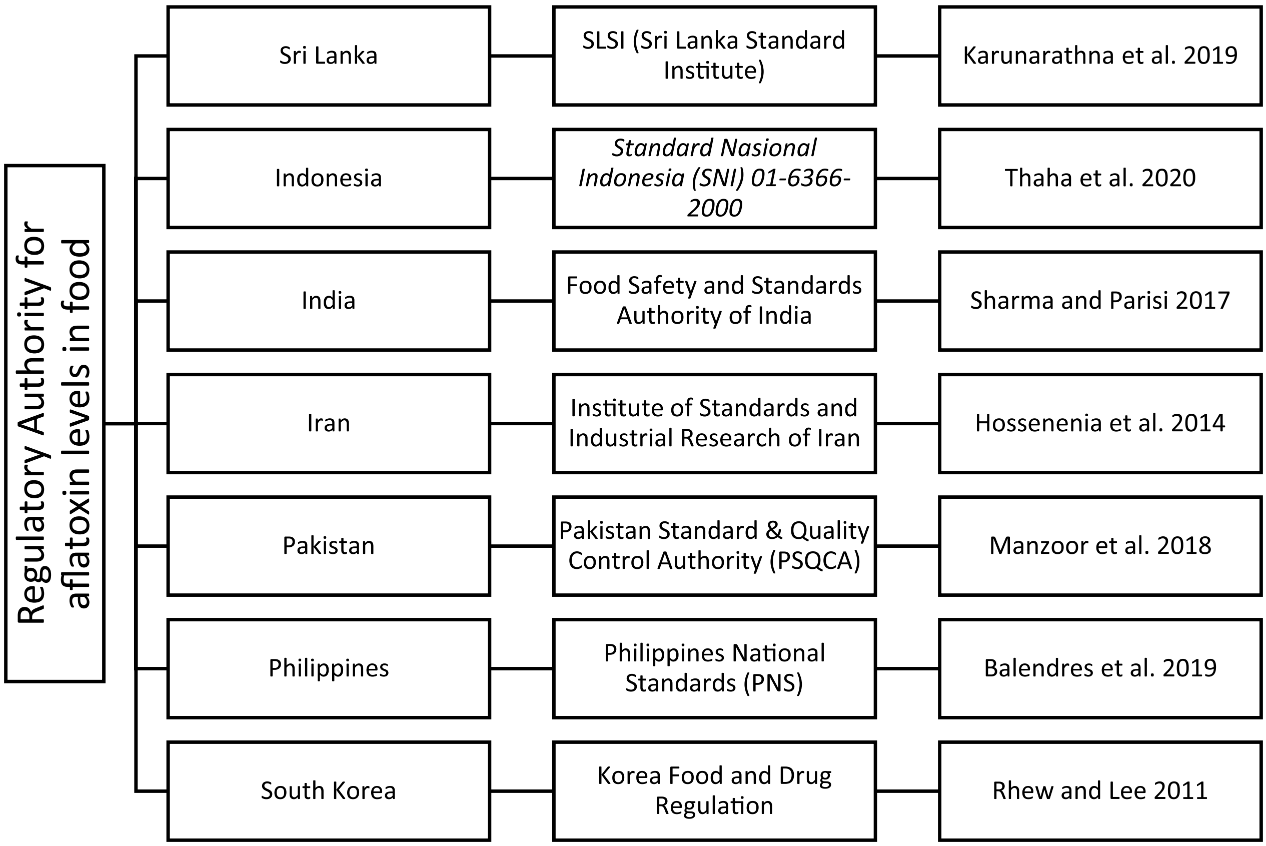

Fig. 3 List of regulatory authorities in various Asian countries

Table 5 Maximum levels of aflatoxin contents safe for human use set by EU and FDA (Van Egmond and Jonker 2004; Robens and Cardwell, 2003)

S. no	Commodity	Maximum level of AFB1 (EU)	Total maximum level (EU)	Maximum level of AFB1 (FDA)	Total maximum level (FDA)
1	Ground nuts and other oil seeds	2 ppb	4 ppb	20 ppb	30 ppb
2	Cereal and cereal products	2 ppb	4 ppb	20 ppb	30 ppb
3	Milk and milk products	-	0.05 μg/kg	-	0.5 ppb

Factors effecting aflatoxin production

Aflatoxin contamination greatly depends upon the geographical distribution due to differences in climatic conditions and the preference of food commodities by different ethnic groups and nations (Lakshman et al. 2022).

Fungal growth significantly depend on biotic and abiotic, which include temperature, humidity, pH, damage by pests, drought etc. (Miraglia et al. 2009; Prandini et al. 2009). The world is also facing another serious issue of global warming, which has resulted as increase in temperature and humidity content of the atmosphere of Earth. These conditions provide favourable conditions for *Aspergillus fungi* to proliferate and consequently produce aflatoxins (Adhikari et al. 2020; Khodaei et al. 2021).

The species *A. flavus* is quite resilient to climatic conditions due to its evolved mechanisms survive and adapt to changing climatic conditions. (Nesci et al. 2004; Medina 2014).

Aflatoxins can also contaminate during post-harvest if the storage conditions are not adequate (Payne 1992). It was found out that aflatoxin prevalence in Pakistan is higher in winters, followed by spring, autumn and lower in summers (Ismail et al. 2016). Climate change in Europe has led to an increase of almost 2 °C temperature allowing proliferation of *Aspergillus* and contamination of aflatoxins in the region (Battilani et al. 2016). The projected climatic change favors the growth of toxin producing *Aspergillus* in cereals and grains with in over the next 30 years posing a significant threat to food security in the region (Moretti et al. 2019).

Management of aflatoxins

Aflatoxins can contaminate the crops both before and after harvest. However, some conditions provide predisposing factors for *Aspergillus* growth; like dry environmental conditions at crop maturity onset, high moisture content of grains, insufficient drying of commodities and inadequate storage facilities (Stepman 2018). If the rice kernels are not completely dried to a moisture level of less than 14%, then they are more prone to aflatoxin contamination. The contamination also damages the rice grains externally by discoloring the grains and lowering the quality (Oyebamiji et al. 2021).

In both field and storage conditions, groundnuts and beans are highly susceptible to aflatoxin contamination, which are of common use. Further, aflatoxins have also been detected in poultry eggs and cow's milk in Cameroon (Tchana et al. 2010).

In Asia, crops are widely exposed to contaminants at various stages, from farm to fork level due to inadequate understanding and awareness of health concerns associated with the contaminants. The contamination begins at harvest, continues at storage, adds on at production level and finally complements in distribution level. The most economic and common method of drying in Asia is sun-drying, which requires the grains to be spread in open air for long periods. However, this method also potentially exposes the grains to aflatoxin contamination (Lakshman et al. 2022).

Control methods

Aflatoxin biodegradation is relatively difficult because of the resistant nature of the xenobiotic poly-heterocyclic toxins that is resilient to common treatments (Brana et al. 2017). The control of aflatoxin production can be regulated, either by preventing the growth of *Aspergillus* in crops or by decontaminating the affected product (Pleadin et al. 2014; Lavkor and Var 2017; Benkerroum 2020). Prevention and decontamination both can be done at pre-harvest and post-harvest stages of the crops (Kabak et al. 2006; Lavkor and Var 2017). Figure 4 and Table 6 provide a concise overview of the methods that have been devised for the control and mitigation of aflatoxins.

Physical and chemical methods usually have some constraints or adverse effects on the environment; while microbial and enzymatic treatment of aflatoxins provide an eco-friendly and more effective alternatives. Using *Flavobacterium aurantiacum* can remove AFM1 from milk and milk commodities (Peles et al. 2021). Many methodologies

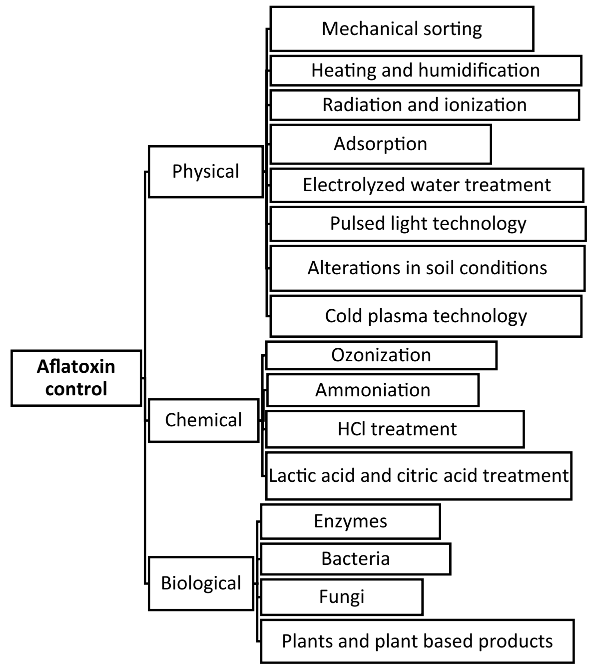

Fig. 4 Methods for aflatoxins control in food commodities

have been devised for the control of aflatoxin contamination, but they are either expensive or harmful for the environment. The current approaches are moving towards a more promising solution that is biocontrol of aflatoxins, which is safe, eco-friendly and less costly.

Similarly, using non-toxigenic strains of *A. flavus* can be used as biocontrol agents to mitigate the aflatoxin contamination by providing a competitive environment to toxigenic species (Dorner 2009; Azmoun et al. 2022).

Biological treatment

Biological control of aflatoxins is a cost effective and ecofriendly method used for mitigating aflatoxin contamination in food and feed stuffs, also to minimize contamination in the food value chain (Bandyopadhyay et al. 2019). This method uses micro-organisms like bacteria, fungi, algae etc. or the metabolites produced by these micro-organisms, like enzymes (Yin et al. 2008). They either degrade the invasive fungi directly or compete with the other microorganisms for food and space. These methods provide products, that are safe for human and animal consumption by reducing the secondary metabolites.

As biocontrol agents, non-toxigenic strains of *A. flavus* themselves act as a counter to control the growth of toxigenic *Aspergillus* species. The non-toxigenic strains of *Aspergillus* lack the polyketide synthase genes that are needed to produce aflatoxins. These strains have been found to be up to 99.3% effective to control the aflatoxin

Table 6 List of methods used to control aflatoxins

S. No	Method	Sub type	Details	References
i	Physical	Mechanical Sorting	• Cleaning • Sorting • Handpicking	Peng et al. 2018; Arzandeh et al. 2011; Mgbeahuruike et al. 2018; Fan et al. 2013; Pérez-Flores et al. 2011; Ogbadu 1980; Rohimah 2021; Kim et al. 2014; Hwang and Lee 2006
		Heating and Humidification	• Roasting • Steaming • Cooking	
		Radiation and Ionization	• UV rays • Gamma rays • Microwaves	
		Adsorption	• Activated carbon • Sorbents • Clay	
		Electrolyzed water treatment		
		Pulsed light technology		
		Alterations in soil conditions	• Farm yard manure • Gypsum • Hydroxide • Bicarbonates • Calcium Chloride	
		Cold plasma technology	• Argon plasma • Radio frequency plasma	
ii	Chemical	Ozonization		Mendez-Albores et al. 2007; Wang et al. 2020
		Ammoniation	Ammonium gas or ammonium hydroxide	
		HCl treatment		
		Lactic acid and citric acid treatment		
iii	Biological	Enzymes	• F-240 dependent reductase • *P. ostreatus* • aflatoxin-detoxifizyme	Peles et al. 2021; Dorner 2009; Zucchi et al. 2008; Campos-Avelar et al. 2021; Holmes et al. 2008; Degola et al. 2017; Zucchi et al. 2008; Sultan and Magan 2011; Campos-Avelar et al. 2021; Holmes et al. 2008; Rohimah 2021; Lillehoj et al. 1979; Mishra and Das 2003; Benkourrum 2020; Motomura et al. 2003; Guo et al. 1997; Munkvold and Hellmich 1999
		Bacteria	• Streptomyces and their isolates • *Achromobacter xylosoxidans* • *Bacillus subtilis* • *Propionibacterium* • *Lactobacillus* • *Enterococcus faecium* • *Streptococcus lacti* • *Rhodococcus erythropolis* • *Bacillus licheniformis* • Strains of *Lactobacillus amylovorus* and *Lactobacillus rhamnosus,* • *Flavobacterium aurantiacum* NRRL B-184	
		Fungi	• *Rhizopus oligosporus* • *Aspergillus niger* • *Eurotium herbariorum* • *Saccharomyces cervesisiae* • Nontoxigenic strains of *Aspergillus*	
		Plants and plant-based products	• Maize inbred Tex6	

production in crops, although proper timing of application and dosage must be ensured for optimum results (Khan et al. 2021).

Bioproducts—the new trend

Using non-toxigenic strains of *A. flavus* reduced the aflatoxin contamination in various crops like maize, cotton and peanut by 67–95%. (Cotty and Bayman 1993; Dorner 2008; Atehnkeng et al. 2014; Mauro et al. 2018).

Aflasafe, an aflatoxin biocontrol product, was used for the first time in maize and is being manufactured by a local supplier for easy availability to local farmers. The product uses sterile sorghum grain, coated with a spore suspension of non-toxigenic strains of *A. flavus* (Senghor et al. 2020). The coating on the grain of sorghum is made by a polymer and the blue color of the product is due to a food-safe colorant, added to differentiate the product from ordinary sorghum grains (Bandyopadhyay et al. 2016).

Aflasafe-SN01 is the first biocontrol product registered for aflatoxin mitigation in Senegal and Gambia (Senghor et al 2021). The term “Aflasafe” is a trademark belonging to the International Institute of Tropical Agriculture (IITA), who manufactured it for use in Nigeria, Senegal, Kenya, Burkina Faso, Gambia and Ghana (Senghor et al 2021). In Africa, the biocontrol product Aflasafe was successfully applied in soil on maize crop, which provided up to 99% efficacy (Kinyungu 2019). The product included non-toxigenic strains of *A. flavus* that inhibit the growth of toxigenic *Aspergillus flavus.* Several bioproducts, under the tradename “Aflasafe” have been registered in Africa and are now commercially available to farmers. After the success in maize, Aflasafe use has been extended to in other crops, like sorghum, sesame, millet and sunflower (Bandyopadhyay et al. 2019; Agbetiameh et al. 2020; Senghor et al. 2020).

A list of bioproducts, registered and not yet registered have been enlisted in Table 7.

Afla-Guard and AF-36 are two biocontrol products in the United States, comprising non aflatoxic strains of *Aspergillus* species, which have also been approved by U.S. Environmental Protection Agency (EPA) as food safe in maize, peanut and cotton seed. Afla-Guard possesses a non-toxigenic strain of *Aspergillus*, NRRL 21882, which was isolated from contaminated peanuts in Georgia (Dorner 2004). Afla-Guard contains strain of *Aspergillus* that does not have the capacity to produce aflatoxins (Lewis et al. 2019). Similarly, AF-36 contains, NRRL 18543, as a non-aflatoxin producing strain of *Aspergillus*, that was originally isolated from Arizona in cottonseed (Cotty 1989).

In South Asia, CABI (Centre for Agriculture and Bioscience International) has taken the initiative to replicate this approach and develop the first biocontrol product in Pakistan named as, AflaPak to manage aflatoxins in maize. In collaboration with Rafhan Maize, National Agricultural Research Centre (NARC) and United States Department of Agriculture (USDA), AflaPak is being evaluated in several maize growing areas (Ajmal et al. 2022).

One world one health

Humans are intricately linked to the over-all health and well-being of ecosystems. This is due to linkage and inter-dependency of all species on each other, for food, shelter, company etc. Therefore, aflatoxin management needs of a multi-disciplinary approach that covers implementing agricultural practices to reduce aflatoxin proliferation, ensuring proper storage and handling of

Table 7 List of bioproducts for aflatoxin control

S.no	Product	Efficacy	Year	Country	Status	Reference
1	Aflasafe SN01	100%	2021	Senegal and Gambia	Registered	Senghor et al. 2021
2	Aflasafe GH01, GH02	99%	2020	Ghana	Registered	Agbetiameh et al. 2020
3	Aflasafe Nigeria	< 80%	2016	Nigeria	Registered	Bandyopadhyay et al. 2016
4	Aflasafe KE01	< 90%	2016	Kenya	Registered	Bandyopadhyay et al. 2016
5	Aflaguard	97.38 to 99.82%	2004	US	Registered	Dorner and Lamb 2006
6	AF36	20–45%	2003	US	Registered	Cotty 2005; Doster et al. 2014
7	AF-X1	> 90%	2018	Italy	Registered	Mauro et al. 2018
8	CT3	86%	2005	Southern U.S	Registered	Abbas et al. 2006
9	K49	60%	2005	Southern U. S	Registered	Abbas et al. 2006
10	Aflasafe BF01	> 96%	2016	Burkina Faso	Not registered	Konlambigue et al. 2020
11	AR27	–	2015	Northern Argentina	Not registered	Zanon et al. 2016
12	AR100G	–	2015	Northern Argentina	Not registered	Zanon et al. 2016
13	AFCHG2	–	2015	Northern Argentina	Not registered	Zanon et al. 2016
14	BN30	–	2008	Africa	Not registered	Cardwell and Henry 2008
15	AF051	–	2008	China	Not registered	Yin et al. 2008
16	FS10	–	2013	China	Not registered	Xu et al. 2013
17	BN30	–	2008	Africa	Not registered	Yin et al. 2008
18	Aflasafe TZ01	–	2017	Tanzania	Not registered	Mahuku 2017
19	Aflasafe TZ02	–	2017	Tanzania	Not registered	Mahuku 2017
20	Aflasafe ZM01 & ZM02	–	2017	Zambia	Not registered	Mahuku 2017
21	Aflasafe MW01 & MWMZ01	–	2017	Malawi	Not registered	Mahuku 2017
22	Aflasafe MZ01 & MWMZ01	–	2017	Mozambique	Not registered	Mahuku 2017
23	AflaPak	–	2020	Pakistan	Not registered	Ajmal 2022

crops and food products, and monitoring aflatoxin contents in both human food and animal feed. One health approach recognizes the interplay between, human, animal and environmental health, enabling a comprehensive response to aflatoxin contamination and ensuring the well-being of all. The available evidence suggests lack of knowledge regarding the extent of aflatoxin problem, associated health risks and mitigation strategies in developing countries. Contaminated food often becomes a component of diets of impoverished populations of the developing countries. Hence, there is need for an initiative to be taken by the scientists and regulatory bodies all over the world to make the food in the plates of every person in this world free of aflatoxin.

Recommendations

Following are some recommendations to minimize the negative consequences caused by aflatoxins in our food chain:

- Raising awareness in Asia about the benefits of eco-friendly biocontrol options and encouraging a transition from chemical to biological ones that can contribute to environment conservation and sustainable agricultural practices
- Developing aflatoxin resistant plant varieties can play an important role to mitigate aflatoxins in crops
- Collaborating with the governments to provide solutions to farmers facilitating access to resources, technical assistance and incentives to promote the adoption of effective measures against mycotoxins
- Establishing a globally recognized standard limit for aflatoxins to promote consistent regulations worldwide and help safeguard public health on a global scale
- Establishing laboratory facilities in developing countries for aflatoxin testing may help early detection, prevention and mitigation of aflatoxin-related risks, ensuring safety of public health
- Designing and developing more bio-control products specifically targeting aflatoxin producing fungi that may be applicable to a wider range of crops

Conclusion

Aflatoxin contamination in food commodities is a serious threat that needs to be controlled worldwide, particularly in developing countries. The best and efficient method to reduce aflatoxin exposure to consumer is to mitigate aflatoxin proliferation at farm level. This is possible by adopting modern sustainable technologies, with the use of bioproducts being a particularly promising option. Bioproducts using non-toxigenic strains of *Aspergillus* have been developed and successfully being applied on various crops in different regions of the world. Similar bioproducts need to be developed in Asia for a sustainable solution against mycotoxins. Rigorous standardized regulations with effective pre and post-harvest measures should be implemented to ensure food safety.

Abbreviations

AFB1	Aflatoxin B1
AFB2	Aflatoxin B2
AFG1	Aflatoxin G1
AFG2	Aflatoxin G2
GIT	Gastro-Intestinal Tract
GDP	Gross Domestic Product
EU	European Union
$AUS	Australian Dollar
UHT	Ultra High Temperature
ISIRI	Institute of Standards and Industrial Research of Iran
EC	European Commission
FDA	Food and Drug Authority
FAO	Food and Agriculture Organization
CA	Codex Alimentarius
SLSI	Sri Lanka Standard Institute
PSQCA	Pakistan Standard and Quality Control Authority
PNS	Philippines National Standards
EPA	Environment Protection Agency
CABI	Centre of Agriculture and Biosciences International
NARC	National Agriculture and Research Centre
USDA	United Stated Department of Agriculture
IITA	The International Institute of Tropical Agriculture
APEDA	Agriculture and Processed Food Products Export Development Authority
FSSAI	Food Safety Services International Group

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