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AFLATOXIN: STRATEGIC MANAGEMENT AND BIOLOGICAL EFFECT ON THE HUMAN HEALTH.

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Abstract : Aflatoxin was first identified as the major fungal toxin in the mid-1960s, contaminating a wide range of human foods including animal feeds. Contamination of food and feed with aflatoxin is a serious food safety concern in poor nations, sometimes due to a lack of detection, monitoring, and regulatory procedures to protect the food supply. In these reviews, papers discussed most typical compounds are AFB1 and AFB2, which may be hydroxylated to become AF-M1 and AF-M2, respectively, and are commonly detected in milk and dairy products. Being the most powerful liver toxin and a class I human carcinogen. Aflatoxin can harm the liver, induce cancer, reduce milk supply, weak the immune system, and cause anemia. Aflatoxin contamination is not a new concern, but its severity is increasing, resulting in major food safety difficulties, significant economic losses, and rising levels of food wastage. It must be recognized as one of the most serious threats to global food security. Now we have many novel technologies to control and management of aflatoxin threats.

keywords **– Aflatoxin, fungus, human health, Food.**

1. INTRODUCTION

1.1 HISTORY

Aflatoxin is a type of a fungus' secondary metabolite these are well known as mycotoxin. Aflatoxin was the first time was discovered in 1960 when approximately 100000 turkeys ill and died in England. That for it is well-known turkeys x disease. After that analysis, many turkeys have found very severe symptoms like liver necrosis intestinal inflammation, etc. (Blount et al., 1961). The most frequent fungus is Aspergillus flavus. Fungal species contaminate foods and feed and produce aflatoxin around the world. Because of its potential to grow as a pathogen and saprophyte in the food supply both before and after harvest, Moreover, it is the primary contaminant during food storage (Lahouar et al., 2015). Contamination of food and feed with aflatoxin is a serious food safety concern in poor nations, sometimes due to a lack of detection, monitoring, and regulatory procedures to protect the food supply. It is believed that over 4.5 billion individuals in underdeveloped countries are chronically exposed to mostly unregulated levels of aflatoxin, which causes significant alterations in immunity and nutrition (Williams et al., 2004).

1.2 What are Aflatoxins?

Aflatoxins are fungal compounds produced by Aspergillus flavus or Aspergillus parasiticus strains. Which are widely found in foodstuff. (Reddy et al., 2011) Aspergillus flavus is the most significant and well-known species in the genus Aspergillus because it produces Afls. AF is one of the most common soil-borne molds on the planet, A. Flavus, is a saprobe capable of thriving on a variety of organic nutrition sources such as plant detritus, animal feed, cotton, compost piles, stored grains, and dead insects (Klich et al., 1998). Aflatoxin is developed in temperatures ranging from 12 to 40 degrees Celsius and requires 3 to 18

percent moisture. Aflatoxins are fungal compounds generated by Aspergillus flavus and Aspergillus parasiticus strains. Aflatoxin is created at temperatures ranging from 12 to 40 degrees Celsius and requires 3 to 18 percent moisture (Duncan et al., 2008).

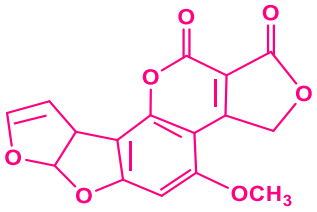
1.3 Types of aflatoxins

The most typical aflatoxins are B1, B2, G1, G2, and M1, M2. Most typical compounds are AFB1 and AFB2, which may be hydroxylated to become AF-M1 and AF-M2, respectively, and are commonly detected in milk and dairy products. Being the most powerful liver toxin and a class I human carcinogen. Aflatoxin can harm the liver, induce cancer, reduce milk supply, weak the immune system, and cause anemia. Furthermore, it has been linked to decreased feed consumption and overall slower growth and development in dairy cattle. Milk output rose by more than 25% when dairy cows were provided an aflatoxin-free diet. Aflatoxin is excreted into milk in the form of aflatoxin M1 within 12 hours, with residues equivalent to around 1.7 percent of the dietary aflatoxin level. The FDA standard for aflatoxin-M1 in milk is 0.5 ppb, whereas the limit for aflatoxin B1 is 20 ppb (Akande et al., 2006). Those four primary aflatoxins are characterized for their fluorescence under ultraviolet light, either blue-(B) or green-(G), and their comparative mobility by thin-layer chromatography on silica gel. Aflatoxin-M1 is a hydroxylated derivative of aflatoxin B1 that cows metabolize and release in milk (Van Egmond et al., 1989).

1.4 Physical and chemical properties of aflatoxin Table 1.

AF. NAME	MOLECULAR FORMULA	M.W	MELTING POINT	UV. ABSORBANCE AMAX (nm)	Fluorescence Emission (nm)
B1	C17H12O6	312	268-269	223	425
				265	
B2	C17H14O6	314	286-289	265	425
				263	
G1	C17H12O7	328	244-246	243	450
				257	
G2	C17H14O7	330	237-240	265	450
				263	

1.5 Structure of aflatoxin



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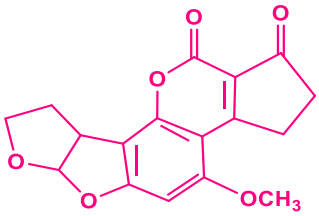

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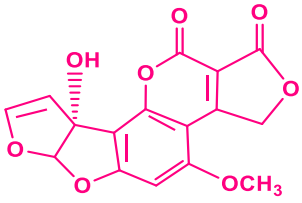
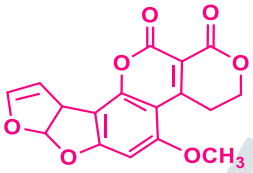
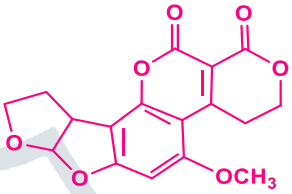


TYPE M1



TYPE G1



TYPE G2

2. FUNGAL PRODUCERS OF AFLATOXIN

Aflatoxin formation and agricultural contamination is a lengthy biochemical process that begins with the invasion of Aspergillus fungus, followed by toxin production in infected crops (Abrar et al., 2013). Fungal attack, growth, and Afs formation in crops are primarily determined by environmental conditions, crop type, and other ecological characteristics of a habitat. (Negash, et al., 2018) Not all Aspergillus species create aflatoxin, and not all Aspergillus species infest all crops. As a result, the fungal ecology of the production field influences the amount and severity of aflatoxin contamination of agricultural products. (Cotty et al., 2006).

2.1 .Section Flavi

This section contains 33 species, the large majority of which are toxic (produce aflatoxin). A. flavus and A. parasiticus are two prominent toxigenic members of the section. Although it was previously thought that A. Flavus only produced B-series aflatoxins, a recent study discovered Korean strains that excrete G-type aflatoxins (Frisvad et al., 2019). A. Flavus is a common soil-borne fungus that feeds on nutrient-rich sources such as organic waste, cereals, and other food resources (Klich et al., 2007). Temperatures between 28 and 37 C are ideal for development, with the ability to stay alive 12 degrees higher or lower.

A. Flavus is not host-specific; it infects a wide-ranging range of food crops (Makhlouf et al., 2019). Parasitic, on the other hand, is more host-specific and has a strong affinity for peanuts (Kumar et al., 2017). Almost all A. Parasiticus strains are toxigenic and produce additional metabolites such as kojic acid and aspergillic acid (Al-Hmoud et al., 2012). Another species in this section that selectively produces aflatoxins B-1 and B-2 is A. Togoensis. (Pildain et al., 2008).

2.2. Section Nidulante

Mainly these categories of species grow in environmental conditions and these three species have distinct growing requirements. Olivicola grows well at 37 degrees C, but A. Astellatus and A. Venezuelensis show little to no growth under the same circumstances. Members of this division are common and are known to actively participate in decomposition processes (Chen et al., 2016).

SECTION	SPECIES	TYPE OF TOXINS PRODUCE	CROPS AND FOOD IT INFACTED	REFERENCES
SECTION FLAVI.	A.FLAVUS	B1,B2,G1,G2	Nuts, cereal	Frisvad et al., (2005)
	A.PARASITICUS	B1, B2, G1, G2	peanuts, maize	Frisvad et al., (2005)
	A.nomius	B1, B2, G1, G2	Wheat	Frisvad et al., (2005)
	A.sergii	B1, B2, G1, G2	Oilseeds, cereals	benkerroum et al., 2020
	A.mottae	B1, B2, G1, G2	cereals	moral et al., 2020
	A. Novoparasiticus	B1, B2, G1, G2	maize	viaro et al.,2017
	A. pseudotamarii	B1,B2	cereals	yoko et al.,2001
	A.arachidicola	B1, B2, G1, G2	Arachis glabrata, Maize	viaro et al.,2017
	A.pseudocaelaelatus	B1, B2, G1, G2	Maize	viaro et al.,2017
	A.transmontanensis	B1, B2, G1, G2	cereals	benkerroum et al., 2020
	A.parvisclerotigenus	B1, B2, G1, G2	peanuts	Frisvad et al., (2005)
	A.aflatoxiformans	B1, B2, G1, G2	cereals	moral et al., 2020
	A. pipericola	B1, B2, G1, G2	cereals	benkerroum et al., 2020
	A.cerealis	B1, B2, G1, G2	cereals	benkerroum et al., 2020
	A.togoensis	B1,B2	cereals	benkerroum et al., 2020
Section nidulante	A.astellantus	B1	cereals and other substrate	benkerroum et al., 2020
	A.miraensis	B1	cereals	benkerroum et al., 2020

3. Occurrence of Afs in Food and Feed

Aflatoxins are di-furanocoumarin derivatives with a bifuran group linked to the coumarin nucleus, a pentanone or lactone ring AFB, and a lactone ring in the aflatoxin. (Schuda et al., 1980). Cereals and cereal-based products are the most common foods consumed by humans globally. Rice and maize are the grains most polluted with aflatoxin. Changes in farming techniques have resulted in natural circumstances. Aflatoxin is produced both during and after harvest. (Hesseltine et al., 1974). According to Filazi and Sireli (2013), rice is more susceptible to aflatoxin contamination than other cereals. Fungal development develops as a result of poor drying of rice grains with a high moisture content (>14%). As a result, these fungi induce discoloration of grain and/or husk and a decrease in grain quality. On the other hand, groundnuts and beans are widely used to augment cereal meals in many African diets. (Soro-yao et al., 2014) However, they are particularly susceptible to aflatoxin contamination in both field and storage environments (Lombard et al., 2014).

The degree of fungal growth and aflatoxin formation in cereals is affected by temperature, humidity, soil type, and storage conditions (Achaglinkame et al., 2017). Furthermore, spices are vulnerable to aflatoxin contamination and are greatly influenced by storage and processing conditions. Aflatoxin-contaminated by a wide-ranging range of spices in the Sultanate of Oman, including black pepper, cardamom, cinnamon, clove, cumin, coriander, and ginger (Elshafie et al., 2002). Aflatoxin was found in eggs gathered from a chicken farm as well as raw cow milk in Cameroon. As a result, the afflicted crops allow aflatoxin to enter the food chain, which is heavily impacted by climatic circumstances (Tchana et al., 2010). The presence of aflatoxin is widespread in a wide-ranging range of foods and feeds. Peanuts, nuts, figs, corn, rice, spices, and dried fruits are among the most impacted foods and feed (Martinez et al., 2019).

3.1 Rice

AFB1 contamination has in recent times been revealed in rice in Sweden, India, Malaysia, Pakistan, Ecuador, Brazil, China, and Canada. Rice had the third greatest incidence of contamination among the studies examined for this study, with an average of 55.4 percent of samples infected with AFB1. In one investigation in Brazil, 187 rice samples were tested for aflatoxins and aflatoxin-producing fungus strains. In these samples, 383 Aspergillus fungus strains were discovered, with 17% of those strains capable of producing type B aflatoxins. Approximately 14% of the rice samples tested positive for aflatoxin contamination, with AFB1 levels ranging from 0 to 63.32 g/kg (Katsurayama et al., 2018**).**

3.2Groundnuts

Recent research into AFB1 contamination in groundnuts has been published. Although peanuts are the most usually detected infected groundnut, other types such as pistachios and hazelnuts have also been shown to be contaminated. Research in Japan discovered measurable quantities of AFB1 in ten out of twenty-one peanut butter samples, albeit concentrations did not surpass 2.59 g/kg. Surprisingly, raw peanut samples examined in the research revealed no aflatoxin contamination (Kumagai et al., 2008).

3.3 Maize

Maize has by far the greatest levels of AFB1 detected. Studies in Croatia, Pakistan, and the Democratic Republic of the Congo, for instance, found maximum AFB1 levels of more than 1000 g/kg (2072, 1405.3, and 1401.45 g/kg, respectively). In the Democratic Republic of the Congo investigation, samples were tested during harvest, during transit, and finally at the market. The frequency of AFB1 infection rose significantly between newly harvested maize (32%), and market samples (100 percent) (Kamika et al., 2016). Both investigations that gathered samples from Pakistan revealed substantial contamination. Found maximum values of 1405.3 g/kg in Lahore, Pakistan, (Firdous et al.). And found maximum levels of 409.3 g/kg in Punjab, Pakistan (Iram et al., 2014).

3.4Wheat/Sorghum/Cereals

Fewer research has lately explored AFB1 incidence in wheat, sorghum, and cereals. Despite only appearing in a few trials, sorghum exhibited the greatest average frequency of AFB1 contamination (67.3 percent) and the second-highest average maximum concentration (83.6 g/kg) among all food items studied (Ghali et al., 2010, Reddy et al., 2011).

4. Metabolism of aflatoxin

AFB1 is processed by the P450 enzyme system in the liver to produce the ultimate carcinogen aflatoxin B1-8, 9-epoxide (AFBO), which contains two isomers: endo-8, 9-epoxide and Exo-8,9-epoxide (K D Raney et al., 1992; Baertschi et al., 1988). CYP3A4

and CYP1A2 are the enzymes that perform this metabolic reaction in the human liver. CYP3A4 is the principal generator of AFBO production at high AFB1 concentrations, creating practically just the exo-isomer of AFBO (Ueng et al., 1995). However, when the substrate concentration is low, CYP1A2 appears to flip to the primary producer of AFBO, implying that at lower AFB1 concentrations, CYP1A2 becomes the main manufacturer of AFBO. Furthermore, at these low doses, CYP1A2 was shown to create more of the exo isomer than CYP3A4 (Gallagher et al., 1996, 1994). This intermediate's strong electrophilicity allows it to react spontaneously with biological amines in proteins and nucleic acids. When AFBO reacts with DNA, it forms the adduct AFB1-N7-guanine by binding covalently to the N7 site on guanine. Because the exo-isomer has a far greater affinity for guanine residues than the endo-isomer, AFB1-Exo-8, 9- epoxide is thought to be the most cancer-causing metabolite (Essigmann et al., 1977) (Gopalakrishnan et al., 1989) (Iyer et al., 1994) (Johnson et al., 1997).

4.1 Hydroxylation products

The P450 system also metabolizes AFB1 into a multitude of hydroxylation products. Aflatoxin-M1, aflatoxin-Q1, aflatoxin-P1, aflatoxicol, aflatoxicol-H1, and aflatoxin B2a are examples of these (AFB2a). AFM1 is a significant metabolite generated by CYP1A2 that is frequently seen in people and animals that have been exposed to AFB1. The hydroxylated metabolite AFM1 is showing the most carcinogenic among the hydroxylated metabolites, causing cancers in rainbow trout and rats **(**Slnnhuber et al., 1974; Cullen et al., 1987). The DNA binding ability of AFM1 has been proven in rats, mice, and pigs, and it has even been discovered to generate an N7 guanine adduct similar to AFB1 (Egner et al., 2003; Lutz et al., 1980). AFM1 is often found in dairy cow milk and humans, opening up a slew of dietary exposure possibilities (Giovati et al., 2015). Following AF-B1 exposure, AF-M1 is likewise excreted in high amounts in urine and therefore has become another biomarker of AF-B1 exposure (Ross et al., 1992).

AF-Q1 is another hydroxylated metabolite that appears to be generated primarily by CYP3A4 (Gallagher et al., 1996, 1994). This metabolite was initially discovered in monkey liver microsomal preparations exposed to AFB1, where it was created in far greater quantity than AFM1 (16-52 percent of substrate for AFQ1 vs. 1-3 percent for AFM1), even though rat microsomes produced far less AFQ1 (Masri et al., 1974). Human livers from biopsies or autopsy were utilized to prepare microsomal preparations to evaluate the metabolic conversion of AFB1 to AFQ1. When AFB1 was introduced into these microsomal reaction mixtures, 18 of the 22 samples produced AFQ1. The abundance of AFQ1 ranged from 1 to 11 percent of the original quantity of AFB1, demonstrating that AFQ1 is produced often and at high enough quantities in people to be detected (Yourtee et al., 1987).

Furthermore, AFQ1's DNA binding capacity was found to be significantly lower than that of AFBO, indicating that, unlike AFM1, it may be used as a detoxifying product (Kevin et al., 1992).

5. Mechanism of action of aflatoxins

Aflatoxins are highly lipid-soluble chemicals that are easily absorbed into the bloodstream from the site of exposure, often through the gastrointestinal system and respiratory tract. . Humans and animals are exposed to aflatoxins through two principal routes: (a) direct consumption of aflatoxin-contaminated foods (b) ingesting of aflatoxins carried over from feed into milk and milk products such as cheese and powdered milk, as well as other animal tissues, mostly as AFM1. (Agag et al., 2004)

When aflatoxins enter the body, they are absorbed through cell membranes and enter the bloodstream. They are delivered in the circulation to many tissues as well as the liver, the primary organ of xenobiotic metabolism. Aflatoxins are mostly processed by the liver to a reactive epoxide intermediate or hydroxylated to form the less dangerous aflatoxin M1. Aflatoxin-8,9-epoxide, a reactive form that binds to DNA and albumin in the blood serum, producing adducts and thereby causing DNA damage, is processed by cytochrome P450 (CYP450) microsomal enzymes in humans and vulnerable animal species. In the liver, several CYP450 enzyme isoforms convert aflatoxin into a reactive oxygen species (aflatoxin-8, 9-epoxide), which can subsequently attach to proteins and produce acute toxicity (aflatoxicosis) or to DNA and trigger liver cancer (Wild et al., 2009 Khlangwiset et al., 2010).

5.1 Aflatoxins' effect on mitochondrial DNA

All through hepato-carcinogenesis, the reactive aflatoxin-8,9-epoxide preferentially binds to mitochondrial DNA (mitDNA) rather than nuclear DNA, inhibiting ATP production and FAD/NAD-linked enzymatic functions, resulting in the disruption of mitochondrial role in the various parts of the body that require the production of energy in the form of ATP. (WHO. Retrieved 2008).

AFB1 attaches to DNA, causing structural DNA changes that result in gene mutations as well as changes in the length of telomeres and cell cycle checkpoints. The reactive aflatoxin-8, 9-epoxide can affect the cell cycle's mitotic (M) phase, growth process (G1 and G2 phases), and DNA synthesis (S phase) by disrupting the various checkpoints that regulate cell cycle development and proliferation, resulting in cell deregulation and, ultimately, cancer development (Vermeulen et al., 2003).

5.2 Aflatoxins' effect on mitochondrial structure

Aflatoxin alters mitochondrial ultrastructure. AFB may also disrupt telomere length and the numerous checkpoints in the cell cycle, causing further harm to the cell cycle's regulatory systems. It also causes mitochondrial-directed apoptosis, which reduces mitochondrial activity (Hornsby et al., 2007).

5.3 The role of the cytoplasmic reductase enzyme in AFB1 detoxification

AFB1 is also converted to other classes of metabolites in hepatocytes by cytoplasmic reductase, such as aflatoxicol, and by the microsomal mixed-function oxidase system to form AFM1, AGFQ1, AFP1, and AFB1-epoxide (these are shown the maximum toxic and carcinogenicity), and these metabolites can be deposited in different body tissues and also edible animal products (Sherratt et al., 2001) (Stewart et al., 1996).

5.4 Role of Aflatoxins in cancer

Aflatoxins, specifically AFB1, AFG1, and AFM1, are the maximum dangerous naturally occurring carcinogens, with AFB1 being the most hepatocarcinogenic toxin, causing cancers of the liver and other bodily organs in the humans and animals (Kitya et al., 2009) (INCHEM Principles 1993).

The capacity of aflatoxin to build altered forms of DNA adducts leads to its cancer-causing potential. Hepatocellular carcinoma is the principal illness linked to aflatoxin intake (HCC, or liver cancer). This illness is the world's third-biggest cause of cancer mortality (WHO. Retrieved 2008) (Beckingham et al., 2001). The association of Aflatoxin B1, the most prevalent and powerful of the aflatoxins, with a particular AGG to AGT amino acid transversion mutation at codon 249 of the p53 gene in human HCC (Hepatocellular carcinoma) provides mechanistic support for a causal link between exposure and disease (Wild et al.,2009,) & (Wu, F., & Khlangwiset, 2010).

5.5 Aflatoxins' effect on the human and animal health (Aflatoxicosis)

All animal species are vulnerable to aflatoxicosis, and individual animal susceptibility varies greatly depending on dose, exposure duration, species, age, sex, and diet. When protein and protein-free diets were provided separately, AFB1, AFB2, and AFM were found in the liver, gall bladder, spleen, heart, muscle, and kidney of developing pigs (Murthy et al., 1975). Aflatoxins promote immunosuppression in animals and also interfere with protein metabolism and numerous micronutrients that are important for health owing to adduct formation. Mutations, cancer, immunosuppression, lung harm, and birth abnormalities are all caused by these adducts (Wallace et al., 1997).

In animals, aflatoxins induce liver damage, reduced milk production, reproductive problems, and immune suppression when consumed in low dietary quantities. In animals, the aflatoxicosis syndrome can also cause vomiting, stomach discomfort, pulmonary edema, convulsions, coma, and death due to cerebral edema and fatty involvement of the liver, kidneys, and heart. Acute toxicosis symptoms in dairy and the beef cattle include anorexia, depression, a dramatic drop in milk production, weight loss, lethargy, GIT dysfunctions like as ascites, icterus, tenesmus, abdominal pain, bloody diarrhea, decreased feed consumption and efficiency; weight loss, jaundice, abortion, hepatoencephalopathy, blindness, walking in circles, ear twitching, frothy mouth (Thrasher et al., 2012, Agag et al., 2004).

6. THE BIOLOGICAL EFFECTS OF AFLATOXINS ON THE BODY ORGANS

Aflatoxins have been shown to impact a variety of bodily organs, including the liver, kidneys, lungs, brain, testes, and numerous endocrine and exocrine organs, as well as the heart, skeletal muscles, and many-body systems.

6.1 Aflatoxins' role in hepatic and other organ and tissue injury

Aflatoxins have been linked to both liver cirrhosis and liver cancer. Acute or chronic hepatic damage can be caused by a range of toxic factors such as chemicals and medicines, trauma, and infectious pathogens (Thrasher et al., 2012). The decreased level of total protein is indicative of AFB1's toxic effect on the liver due to protein synthesis failure, as aflatoxins are known to impair protein biosynthesis by the formation of adducts with DNA, RNA, and proteins, inhibit RNA synthesis, DNA-dependent RNA polymerase activity, and cause endoplasmic reticulum degranulation (Sharma, V., et al. (2011), (Wangikar, P. B., et al. (2005).

Acute hepatic injury caused by aflatoxin results in an increase in serum enzymes such as aspartate aminotransferase, lactate dehydrogenase, glutamate dehydrogenase, gamma-glutamyltransferase, and alkaline phosphatase, as well as other biochemical changes such as proteinuria, ketonuria, glycosuria, and haematuria (.Johnson, W. W., et al. (1997). Aflatoxins, N. L. M. (2002).

6.2 Effect of aflatoxins on the GIT

The gastrointestinal tract (GIT) is the primary pathway via which aflatoxins enter the body as a result of consuming aflatoxin-contaminated foods, particularly AFB1. It is also the primary mechanism via which aflatoxin metabolites are excreted from the bile. Aflatoxin, metabolites, and AF-8, 9-epoxides have been linked to intestinal tumors, particularly human colon malignancies such as colon carcinomas, and comparable results have been shown in experimental animals (Coulombe et al., 1994). Aflatoxins have been linked to digestive issues such as diarrhea, vomiting, intestinal bleeding, liver necrosis, and fibrosis (Harriet, A. M. 2003).

6.3 Effect of AF on the CNS

The neurons in the brain or central nervous system have a high metabolic rate but the minimal ability for anaerobic metabolism, and as a result, insufficient oxygen delivery to the brain kills the neuronal brain cells within minutes. Some substances are neurotoxic or cause harm to neurons, impairing their function. Mycotoxins, especially aflatoxins and their metabolites, as well as other products such as reactive oxygen species (ROS) like AFB-8,9-epoxides, can disrupt normal nerve cell function by forming DNA adducts, protein adducts, oxidative stress factors, mitochondrial directed apoptosis of nerve cells, and inhibiting protein, RNA, and DNA synthesis [(Johnson, W. W., et al. 1997), (Brown, K. L., et al. 2009),(Ezekiel, C. N., et al. 2011) (Halliwell, B. 2007) (Thrasher et al., 2012)]. Aflatoxin reduces dopamine, and serotonin, and alters the levels of the precursor's tyrosine and tryptophan. [Columre al., 1985 Weekley et al., 1989].

Neurotransmitter deficiencies cause neurological symptoms like neurocognitive decline and sleep cycle disruption, as well as symptoms of brain damage such as dullness, restlessness, muscle tremor, convulsions, loss of memory, epilepsy, idiocy, loss of muscle coordination, and abnormal sensations [(Harriet Et al., 2003) (Lukewarm et al., 2004)]. AFB1 has also been shown in experimental animals to enhance central and peripheral nervous system Na+/K+ ATPase, glucuronidase, and galactosidase while inhibiting Mg2+-ATPase, which is critical in the appropriate functioning of glutamate neurotransmitters and their NMDA receptors [Ferreira, I. L., Duarte, C. B., & Carvalho, A. P. (1999). Coulombe, R. A., & Jr, (1994) Arundine, A., & Tymianski, M. (2004).].

6.4 Aflatoxin effects on the CVS

Aflatoxins have been shown to have substantial acute effects on the cardiovascular systems, including vascular fragility and tissue hemorrhaging (Gursoy et al., 2008). In addition to cardiac damage and teratogenic consequences Aflatoxin intake in contaminated foods has been linked to a decrease in protein content of these tissues and organs, as well as a blockage of their metabolic activities[(Mohammed et al., 2009) (Wangikar, P. B., et al. 2005)].

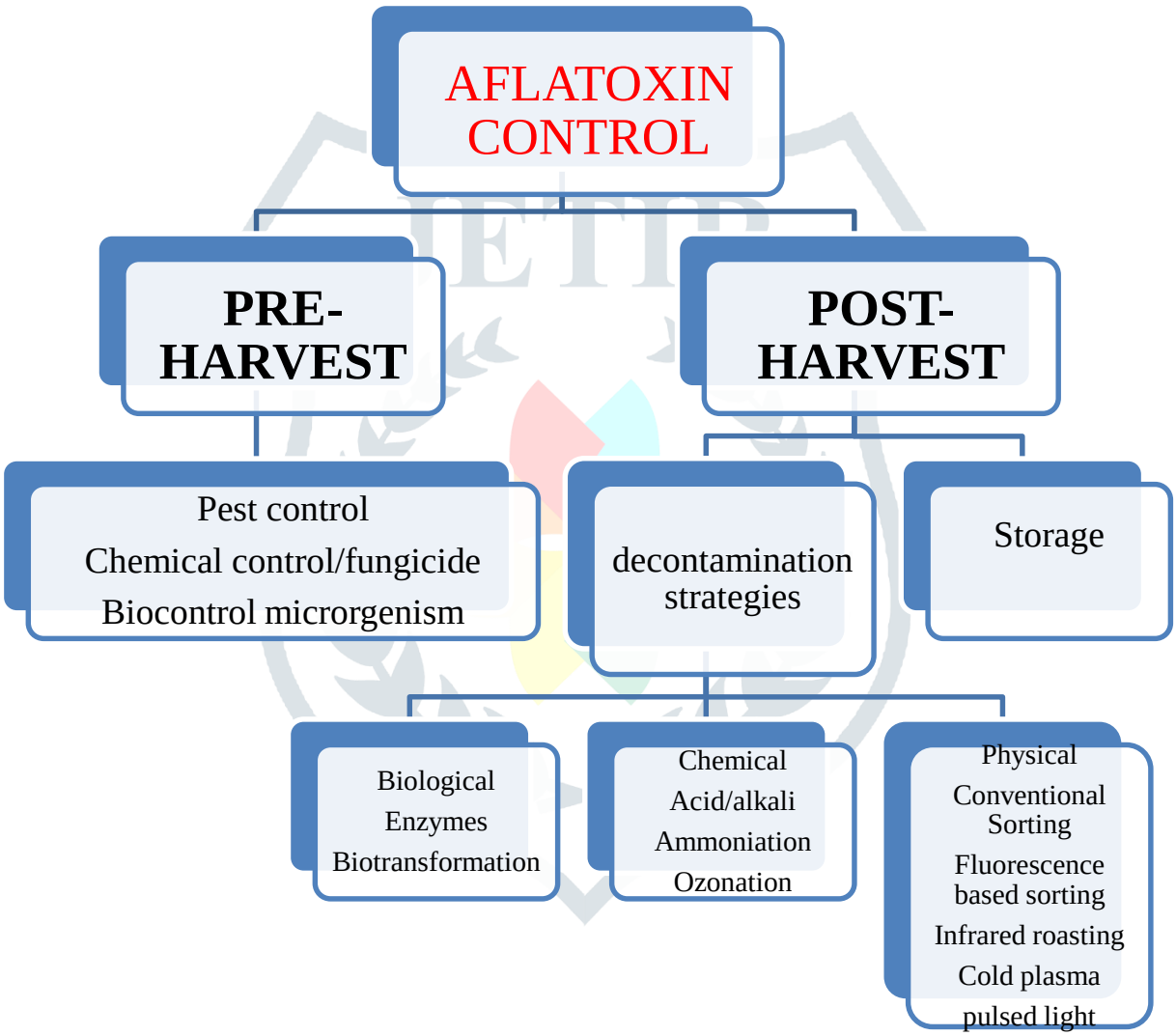
6.5 Aflatoxin's effect on the immune system

Chronic intake of AF-contaminated foods has been linked to immune suppression in both humans and animals globally (Harriet et al., 2003). Aflatoxin affects both the cellular and humoral immune responses in humans, where they modify immunological parameters in individuals with high AFB1 levels, resulting in deficits in cellular immunity and decreasing host resistance to infections [Jiang et al. 2005 Sahoo et al., 1996]. Aflatoxin reduces the amounts of immunoglobulin's IGM, IGG, and IGA in birds, as well as complements activity in hens (Giambrone et al., 1978). AFB1 at low doses reduces both mRNA and protein

levels of lymphocytic IL-2 and it predominantly impacts macrophage functions as well as IL-1, IL-6, and TNF production by these cells (Dugyala et al., 1996).

7. AFLATOXIN MANAGEMENT WITH AN INTEGRATED APPROACH

The Aflatoxin Safe Initiative creates aflatoxin management solutions based on biocontrol that is adapted to the needs of target nations. Any feasible, effective technique or approach is used to synergize their benefits. Implementing customized management measures can result in reliable, cost-effective supplies of aflatoxin-free crops. Crops cultivated, processed, and stored using conventional methods often contain fewer aflatoxins, sometimes up to 100 percent less (Bandyopadhyay et al., 2019, Agbetiameh et al., 2020, Senghor et al., 2020, 2021).



7.1 Awareness and sensitization campaigns

The lack of understanding about aflatoxins and their impact, as well as control measures, among farmers, processors, agricultural and health authorities, regulators, and consumers, is a key hurdle to the implementation of aflatoxin management solutions across SSA (Udomkun et al., 2017). It is essential to construct sensitization efforts that take into account the context of target regions/countries to raise public knowledge of aflatoxins.

7.2 Improved pre-harvest practices

Several variables may lead to increased contamination even before the crop reaches the reproductive stage. Improved seeds, good ground preparation, suitable planting date, correct spacing, appropriate fertilizer, weed management, irrigation if available, and insect control are all encouraged as ways to prevent plant stress and harm. Plant stress and insect damage are decreased as a result

of these techniques, resulting in lower aflatoxin levels (Munkvold, 2003) (Diao et al., 2014) (Seetha et al., 2017) (Mahuku et al., 2019).

Before Aspergillus populations start to grow, biocontrol using aflatoxin is used. During crop blossoming, when crop biomass becomes easily accessible, natural fungal increases are common. As a consequence, two to three weeks before blooming, toxigenic fungi are applied, and aflatoxin producers are displaced. Because fewer aflatoxin producers are linked to treated crops, fewer aflatoxins accumulate, and often none at all (Horn et al., 2000) (Cotty et al., 2007) (Agbetiameh et al., 2020).

7.3 Improved harvest and post-harvest practices

Aflatoxin levels rise dramatically throughout storage, transportation, and until the crop is consumed when improper harvest and post-harvest methods are used. (Aidoo et al., 1993) (Hell et al., 2008). Farmers and farmer trainers are so trained to harvest crops as soon as they are ready. Trainees are made aware of the dangers associated with: I) early harvesting- high moisture content, increased drying time, and sensitivity to mold development during storage; and ii) postponed harvesting- loss of quality, unwanted exposure to birds, rats, and/or rain, all of which can promote to fungal growth and aflatoxin generation. It is advised that harvested crops be dried immediately to a safe moisture level of 10 to 12 percent (Diao et al., 2014).

Maize farmers are recommended to avoid harvesting cobs from stuck plants due to the risk of coming into contact with aflatoxin manufacturers in the soil, as well as to separate healthy corn from immature, insect- or rodent-damaged, or sick cobs. Farmers who stack plants to dry should keep the heaps erect, producing a cone, and prevent large heaps that may tumble and/or accumulate moisture in the middle. Other suggestions include placing seeds in clean bags and avoiding soil contact. To reduce the tendency to fungal development during storage, groundnut growers are recommended to avoid damaging the pods during removal and to transfer selected pods into clean containers.

7.3.1 Decontamination strategies

A. Sorting

Hand sorting is still the most common way of removing aflatoxin contamination, particularly in less economically developing nations (Matumba et al., 2015). Since the late 1800s, many types of sorting machines have been in use (Karlovsky et al., 2016). Originally segregated samples were based on their weight and size, but technology has evolved tremendously since then. Machine sorting based on pre-defined physical features (colour, size, and density) has been proved in studies to be successful. In which any sample that deviates from the predetermined limits is rejected and removed (De Mello and Scussel, 2009)

Fluorescence sorting is a novel technique that allows for analysis at a scale that reduces the danger of aflatoxin contamination while also minimizing food waste. It is generally known that aflatoxins may be detected using ultraviolet (UV) light. Aflatoxin contamination is identified using the Bright Greenish Yellow Fluorescence (BGYF) test as a presumptive test. The BGY-fluorescence is caused by an interaction between kojic acid generated by A. flavus or A. parasiticus, aflatoxin forming fungus, or the mycotoxin itself, and the peroxidase enzyme found in plant tissues (Bühleret al., 2018)

The BGY-fluorescence is caused by an interaction between kojic acid generated by A. flavus or A. parasiticus, aflatoxin-producing fungus, or the mycotoxin themselves, and the peroxidase enzyme found in plant tissues. As a consequence of technological advancements, a unique platform for significantly reducing aflatoxin contamination in maize has been developed. This method takes advantage of the fluorescent properties of kojic acid and combines a camera designed and optimized using hyperspectral fluorescence data with an LED-based UV lighting system to detect and sort out contaminated kernels at a rate of 15 tonnes per hour, with a reduction in aflatoxin contamination averaged nearly 85-90 percent in tests to date. However, non-contaminated production losses are less than 5% (Bühler, 2018).

B. Ozone

Ozone may be sprayed in three distinct ways throughout the cleaning process: dry, wet, and moist (Mallakian et al., 2017).

Aflatoxin breakdown by ozone occurs as a result of an electrophilic assault on the C8-C9 double bond of the furan ring in its molecular structure, resulting in the creation of primary ozonize, which are then rearranged into aldehydes, ketones, and organic acids (Jalali et al, 2016).

C. Cold plasma

Cold plasma is a distinct type of the fourth state of matter and new technology with enormous promise in a variety of food-related applications. Plasma is a quasi-neutral ionized gas that consists largely of free electrons, photons, and ions (Pankaj et al., 2014). Plasma may be formed using various temperature and pressure ratios and categorized into two categories: thermal and non-thermal plasma. Thermal plasma is created under high pressure and high power, resulting in plasmas with high temperatures and homogeneous electron and neutral species distributions (Eliasson et al., 1991) (Scholtz et al., 2015).

7.4 Improved storage structures, use of hermetic bags

The kind of storage structure has a big impact on post-harvest aflatoxin levels. (Hell et al., 2000; Aidoo, 1993). Farmers are encouraged to build structures that are well-ventilated and have sturdy, well-built walls and roofs to prevent rain seepage and excess moisture. Before storing new crops, farmers should repair, fumigate, and clean the buildings. Insect and rodent control is stressed to minimize crop quality loss and spoiling. The use of hermetic bags and silos has been shown to successfully inhibit the development of aflatoxin during storage. (Walker et al., 2018; Danso et al., 2018)

7.5 Enhance the ability to control and decrease health consequences

Crops protected by integrated aflatoxin management have fewer aflatoxins than non-protected crops, often up to 100 percent less. Farmers' ability to adopt technology that limits aflatoxin prevalence and exposure has improved. As a result of protecting crops from aflatoxins, there is an indirect decrease in and control of health risks.

CONCLUSIONS

Aflatoxin contamination is a prevalent problem in both humans and animals across the world, particularly in poor developing countries in Southeast Asia and Sub-Saharan Africa, where inadequate food collection, processing, and storage of food and food items allows mold to grow on them. Aflatoxins, their metabolites, aflatoxin-8, 9-epoxide, and the produced (reactive oxygen species) ROS have negative effects on numerous bodily organs and systems, including the development of malignancies, particularly liver cancer, which is mostly caused by AFB1 exposure. Aflatoxins also reduce humoral and cell-mediated immunity, making people more vulnerable to serious diseases. Aflatoxins also cause malabsorption of numerous minerals, resulting in nutritional deficiencies, poor immune function, malnutrition, and stunted growth in babies, leading to the development of kwashiorkor and marasmus. Aflatoxins may damage all of the body's systems, and therefore the health of those who are exposed to them, particularly in impoverished developing countries such as Southeast Asia and Sub-Saharan Africa, where inadequate food collection, processing, and storage allow mold to grow.

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