Review Article

Exposure to Mycotoxins and its importance in public health

Abstract

There are a wide variety of toxic compounds that are produced by fungi, known as mycotoxins, which are extremely important because they are found as contaminants in food for human and animal consumption, mycotoxicoses are diseases caused by mycotoxins, exposure to it occurs by ingestion, by skin contact and inhalation, which cause adverse damage to human and animal health, these effects cost millions of dollars annually in global losses in human and animal health, as well as in agricultural products, some mycotoxins of importance in public health they include aflatoxins, trichothecenes, fumonists, ochratoxins, among others.

Keywords: *aflatoxins, aflatoxigenic foods, effect, mycotoxigenic*, Fumonisins, *mycotoxins*, Trichothecenes, Ochratoxin.

Introduction

Mycotoxins are secondary metabolites produced by different genera and species of fungi, the main ones being Aspergillus spp., Fusarium spp. and Penicillium spp. that colonize and contaminate substrates used in human and animal food (Council for Agricultural Science and Technology, 2003).

These effects on animal and human health are known as mycotoxicosis, the severity of which depends on the toxicity of the mycotoxin, the degree of exposure, the age, the nutritional status

of the individual, and the possible synergistic effects of other chemical agents to which the individual is exposed (Peraica et al., 2000).

The consumption of a contaminated diet produces acute and chronic effects; generally the effects are teratogenic (birth defects during gestation), carcinogenic, estrogenic and immunosuppressive (Abrunhosa et al., 2014). There are other reported effects such as neurotoxicity, nephrotoxicity, hepatotoxicity, myelotoxicity, pulmonary and endocrine toxicity (Marroquín et al., 2014; Gimeno and Martins, 2011), the most important mechanisms for the occurrence of such manifestations are oxidative stress and mycotoxin-induced genotoxicity (Hope, 2013).

Mycotoxicosis has been described since ancient times and for some researchers it was the cause of the last of the ten plagues of Egypt (González Salgado, 2010). The first documented cases of these intoxications date back to the Middle Ages in Europe where this clinical picture was called ¨fire from hell¨, due to hallucinations, psychosis, delirium, convulsions, burning sensation, and distal necrosis (González Salgado, 2010; Beardall and Miller, 1994).

The general interest in mycotoxins increased in 1960, when a feed-borne mycotoxicosis in farm animals in England was reported as turkey "X" disease, which was later found to be caused by aflatoxins (Peraica et al, 2000).

There is a long tradition of the use of some molds in the production of cheese and salami, as well as in the fermentation of beer and wine, and in the pharmaceutical industry in the manufacture of antibiotics. The classification of mold metabolites as antibiotics or as mycotoxins is based on their toxicity or therapeutic effects. There are some mold metabolites initially considered as antibiotics that later turned out to be very toxic, such as Citrinin, which is now classified as a toxin (Reiss, J., 1978).

Mycotoxins are produced mainly by filamentous fungi under optimal temperature conditions ranging from 20 - 25°C, requiring a pH between 4 and 8 and a relative humidity of 80 - 90% (Murray et al., 2009). Currently, more than 400 toxins produced by 350 species of fungi have been isolated and characterized; of these, research has focused on those that cause significant damage in humans and animals (Brase et al, 2009).

The effects of mycotoxins cost millions of dollars annually in worldwide losses in human and animal health, as well as in agricultural products (Vasanthi & Bath, 1998). Some mycotoxins of public health importance include aflatoxins, trichothecenes, fumonists, ochratoxins and zearalenone (Abrunhosa et al., 2014).

This review analyzes the different types of mycotoxins that report effects on human health and are of public health importance.

Aflatoxins

Aflatoxins are a group of approximately 20 compounds produced by species of the genus Aspergillus. The term "Aflatoxin" was coined in England in the 1960s, when thousands of turkeys were fed peanut meal contaminated with the mycotoxin and died from an unknown disease that was called turkey "X" disease (Blount, 1961).

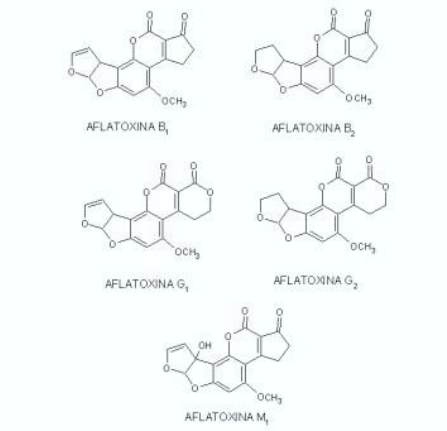
They are carcinogenic, teratogenic, mutagenic mycotoxins, which have tropism for organs such as liver, brain, and kidney. These toxins are produced under optimal conditions of temperature and humidity (Shan and Williams, 2014). They are produced in nuts, cereals, and rice and constitute an under-recognized human health risk, the two most important aflatoxin-producing species of Aspergillus are Aspergillus flavus, which only produces aflatoxin B, and Aspergillus parasiticus, which produces aflatoxins B and G. aflatoxins M_1 and M_2 are oxidative metabolites of aflatoxins B_1 and B_2 produced by animals after ingestion of these , they appear in breast milk, (both animal and human), urine and feces (Ruvalcava et al, 2014), aflatoxin B_1 is the most toxic of all, and has been correlated with hepatocellular carcinoma in humans and in a wide variety of animal species (Richard, 2007; Wu et al., 2014), as depicted in Figure 1.

Aflatoxin B_1 (AFB1) is a common contaminant in tropical and subtropical climates of stored foods (peanuts, pistachios, corn and rice), this mycotoxin has been described as a potent dietary carcinogen and is implicated in the etiology of hepatocellular carcinoma, it has also been associated with immunosuppression and severe nutritional deficits (Abaroa Aguirre et al, 2015; Yunus et al, 2011; Gross and Eaton, 2012).

Intoxication with this toxin is called aflatoxicosis, and there are two clinical forms: acute and chronic. The acute form is related to nephrotoxicity, cardiotoxicity and hepatotoxicity and the chronic form is related to protein malnutrition, carcinogenesis and immunosuppression, because these substances induce thymic aplasia, affect the number and function of lymphocytes, inhibit phagocytosis, reduce complement activity and decrease IL-2 expression, as a result of permanent exposure to sublethal doses of this mycotoxin (Yard et al., 2007).

Its toxicological mechanism is based on its epoxide radical which interacts with conjugated proteins to produce toxicity and inhibition of protein synthesis, in addition to which it can produce genotoxicity and induce carcinogenic events due to mutation of the P53 gene, with the conversion of guanine to thymine at codon 249 (Murray et al., 2009).

FIGURE. 1CHEMICAL STRUCTURE OF AFLATOXINS B1, B2, G1, G2 AND M1.



Source: Aflatoxins: incidence, health impacts control and prevention. 2014. https://www.researchgate.net/profile/Marcela-Martinez-Miranda/publication/317503564/figure/fig1/AS:613945794641955@1523387492709/Figura-1-Estructura-quimica-de-las-aflatoxinas-B1-B2-G1-G2-y-M1.png

Health Impacts

Mycotoxins have acute toxic activity on sensitive species that produces inhibition of protein synthesis, Reye's syndrome and Kwashiorkor especially in children in the tropics, immunosuppression, skin irritation, endocrine disruption, acute hepatitis and other metabolic disturbances, the clinical picture includes fatty liver and severe cerebral edema, long term carcinogenic, mutagenic, teratogenic, estrogenic, immunotoxic, nephrotoxic and neurotoxic effects (Urrego and Diaz, 2006).

Mycotoxins usually enter the body through ingestion of contaminated food, although inhalation and direct skin contact are important routes (Urrego & Diaz, 2006; Zahin, 2011). They are absorbed in the gastrointestinal tract due to their high liposolubility and biotransformed in the liver by microsomal enzymes of the cytochrome p450 superfamily (IARC, 2012).

There is evidence of the effect of aflatoxins in animals and humans, it is known that acute outbreaks can cause embryonic death, toxicity to the fetus, contamination of breast milk, umbilical cord damage and low birth weight (Ruvalcaba Ledezma et al, 2014).

Aflatoxin B1 is considered by the (IARC) as an evident carcinogen in experimental animals and has also been classified as a human carcinogen (group I) and is the most important in public health (Duarte & Villamil, 2006). On the other hand, they are also implicated in pathogenesis of other types of malnutrition, such as loss of muscle size (wasting), growth retardation and in experimental animal studies aflatoxins lead to micronutrient deficiencies including vitamins A and D, as well as zinc and selenium deficiencies (Chen et al., 2013).

Ochratoxins

They are a group of toxic secondary metabolites produced mainly by fungi of the genera Aspergillus and Penicillium, which are common contaminants of cereals, coffee, bread and foods of animal origin, five types of ochratoxins have been described: A, B, C. α and β, the most toxic being ochratoxin A (González salgado, 2010).

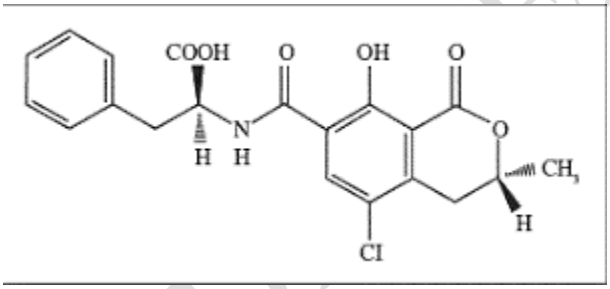
Ochratoxin A (OTA).

As shown in Figure 2, ochratoxin A, a nephrotoxic, carcinogenic, and mutagenic mycotoxin, which is produced essentially by Aspergillus ochraceus and Asperillus nigri species, is soluble in organic solvents and slightly soluble in water, is absorbed in the digestive tract, especially in the small intestine and transported by the circulatory system to the kidneys and in lower concentrations deposited in the liver, muscle and fat (Sorrenti et al, 2013).

They have been shown to have nephrotoxic, hepatotoxic, teratogenic, and immunotoxic effects, as well as having synergism with other nephrotoxic mycotoxins such as citrin (Ostry et al.,2013).

The toxicological mechanism is mediated by inhibition of nuclear factor erythrode~2 (Nrf2) and Nrf2 gene transcription, which generates oxidative stress, production of reactive oxygen species, which induce inhibition of protein synthesis, similarly intervene in metabolic systems, disrupt calcium homeostasis, inhibit mitochondrial respiration and cause DNA damage (Limonciel & Jennings, 2014).

Figure 2.: Chemical structure of Ochratoxin A.



Source: Ochratoxin A in food for human consumption: review. 2011. https://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0212-16112011000600004

Trichothecenes

They are a group of mycotoxins belonging to the genus Fusarium, produced by the species Fusarium tricinctum, Fusarium nivale, Fusarium roseum, Fusarium graminearum, Fusarium solani, Fusarium culmorum and Fusarium poae, have been reported more than 200 derivatives of mycotoxins that are divided into two groups A and B, The most important toxins of group A are T2 toxin, HT-2 toxin, diacetoxyscirpenol, monoacetoxyscirpenol, triacetoxyscripenol and scirpentriol, and

those of group B are vomitoxin, fugarennone X, nivalellol. They are contaminants of cereals and can generate toxicity in animals and humans (Gimeno and Martins, 2011; Ostry, 2013).

The toxicological mechanism is mediated by its interaction with the ribosomal unit 60s, which generates the separation of the rRNA 28s subunit, the blocking of elongation processes and the activation of ribosome inactivating proteins (RIPs), which causes ribotoxic stress and damage to the rRNA, causing inhibition of the translation process and protein synthesis, generating toxicity, inhibition of DNA and RNA synthesis, alteration in cell division, in the membrane structure, besides compromising the integrity and function of the mitochondria (Bin et al., 2011).

Exposure to some of these mycotoxins such as deoxynivalenol and T2 toxin are associated with aleukia toxica alimentativa (ATA), an intoxication characterized by skin inflammation, vomiting, damage to hematopoietic tissues (Bennett and Klich, 2003).

Fumonisins

They are produced by species of the genus Fusarium, being corn the cereal most affected by this group of toxins, although they have been reported in sorghum and rice (Richard, 2007). They were the first mycotoxins implicated in diseases in humans since 1988, later in the United States it was observed that corn contaminated with Fumonisin-producing molds caused the death of hundreds of horses and pigs (Missmer et al., 2006).

According to the International Agency for Research on Cancer (IARC) since 1993, they are classified in group 2B as possible human carcinogens behind AFBI which is in group I of this classification, there are 15 types of Fumonisins grouped into four categories (A, B, C, P) being the best known FB1, FB2 and FB3, of which FB1 is the most toxic (Torres & Lopez, 2010).

Fumonisin B1

This mycotoxin is synthesized during the metabolism of toxinogenic strains of Fusarium verticilloides and Fusarium proliferatum. Intoxications with this toxin have been associated with the consumption of corn and derived foods that are contaminated with small amounts of FB1. In humans, it has been associated with esophageal cancer and neural tube closure defects (Murray et al., 2009; Theumer et al., 2012).

The mechanism of toxicity of FB1 consists of blocking the synthesis of sphingolipids, which are essential elements in the structure of the cell membrane, particularly in nerve cells. This alteration in the biosynthesis of sphingolipids occurs as a consequence of the inhibition of the enzyme ceramide synthetase, which generates the accumulation of compounds such as sphingonine and sphingosine, which produce neurotoxicity, nephrotoxicity and hepatotoxicity (Merrill, 2001).

Conclusions

Mycotoxins are a real problem that affects public health in developing countries, so it is essential to conduct research to mitigate its impact on health, most outbreaks come from food contaminated by mycotoxins so it is necessary to have a strict control on the quality and safety of food, this derived from the techniques and/or methods of determination of this type of toxigenic compounds that by minimal exposure could generate teratogenic-carginogenic impact.

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