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Mycotoxins in foods that cause damage to humans

Abstract

Background: Mycotoxins are toxic substances from the metabolism of RESULTING fungi *Aspergillus* flavus: such as, *Aspergillus* Penicillium, *Aspergillus* ochraceus, Penecillum expansum and Fusarium graminearum. There are four Important mycotoxins: aflatoxins, Ochratoxin A, patulin and deoxynivalenol being responsible for the contamination of food for human consumption.

Methods: The research was Carried out and selected based on inclusion criteria, articles and publications related to mycotoxins, food, toxicity, Mechanisms of action and analysis, published in Scielo, MEDLINE / PubMed, Google academic and Science Direct, to the total of 65 articles Were reviewed, but only 50 met the inclusion criteria above.

Results: The presence of mycotoxins in food remains a public health problem; it is found because worldwide and causes serious pathology in humans and animals both.

Conclusion: it is Necessary to continue advancing in the investigations related to the presence of mycotoxins in food for human consumption, especially regions tropical in, since the environmental conditions and the Characteristics of the food produced in These regions please At least theoretically, the development of These toxins, Which Represents a high risk to the health and food security of the Populations.

Keywords: mycotoxins, (Q000633) toxicity, mechanisms of action, (D000201) analysis, (D005502) food

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Abbrevitations: DON, deoxynivalenol; OTTA, ochratoxin A

Introduction

Mycotoxins are produced by filamentous fungi affecting food (dried fruit, cereals and cereal products, nuts and spices), which are present in the diet of humans secondary metabolites. Various conditions may influence the formation of mycotoxins such as humidity, temperature, oxygen, physical damage to crops and the presence of fungal spores.[1] Mycotoxins are known as toxic compounds which are naturally produced by *Aspergillus* molds spp, Penicillium spp and Fusarium spp, secreting substances such as aflatoxins, ochratoxin A, patulin and deoxynivalenol, which are the most important worldwide, causing diseases in man and animals.[2] Exposure to these mycotoxins can occur directly or indirectly by eating contaminated consumption animals fed with contaminated and particularly by the consumption of milk[3] food. It is therefore that the human being has a potential risk to exposure of mycotoxins.[1]

Moreover, mycotoxins are most dangerous carcinogenic substances produced by the ecosystem, because they are capable of producing mutations in the genetic material of living beings, teratogenic that can cross the placental barrier and damage the fetus, nephrotoxic because in kidney damage, genotoxic as to Cusan DNA damage by changing the transformation of cells and eventually produce malignant tumor, immunosuppressive because it affects and weakens the immune system, hepatotoxic, ie, cause serious damage to the liver.[4] thus becoming a major public health problem which must be prevented and constantly monitor.[4] The purpose of this review article about the main mycotoxins in foods that cause harm to the human, its importance, toxicity, methods of detection and quantitation there of.

Materials and methods

In this review they were taken into account as inclusion criteria published data on mycotoxins in food for human consumption, product of original research and reviews issue further published research were reviewed over a period of time from 2010 to 2018, items in Spanish, English and Portuguese and published in the databases, Science Direct, Scielo, academic google and MEDLINE/PubMed, language a total of 65 articles were reviewed, but only 50 met the inclusion criteria above. Strategy for literature search keywords used were:(Q000633) toxicity (34935) action mechanisms and (D000201) analysis, which are validated in MeSH.

Results

Mushroom producing mycotoxin

Aspergillus spp: It is a fungus that feeds decomposing organic materials, is composed of hyaline septate hyphae of sexual reproduction.[5] Ubiquitous in nature and universal distribution, causes damage in animals and in humans.[6]

The main species of *Aspergillus* fungi that produce mycotoxins in foods that cause diseases in humans are, *Aspergillus* flavus and *Aspergillus* parasiticus;[7] said molds contaminated seed crops mainly cereal grains and before and after harvest during drying, handling and storage.[8] Also produce two important mycotoxins found worldwide and are known as aflatoxins and ochratoxin A, being responsible for massive contamination of foods such as cereals and cereal products, maize and wheat flour.[9]

Penicillium expansum: This fungus is the leading producer of patulin that presents ease to colonize foods like fruits, being

responsible for 70% to 80% of the losses caused by post diseases harvest fruits, mainly apple and a lesser amount in the pear.[10,11]

Fusarium graminearum: Is the most widespread species worldwide, in terms of their morphological characteristics, this fungus has a rapid mycelial growth, reddish pink, sparsely sporulated and sterile aerial mycelium yellowish brown.[12] Moreover, the mycotoxin produced is known as deoxynivalenol, its production is evident when the contaminated food mycelium pink white- colored basal appears presence abundantly sporulation, together with slightly curved hyaline macroconidia with septa, apical cell is pointy and shaped foot.[13]

Mycotoxin: Mycotoxin production is given by various factors, such as drought, lack of soil fertilization, high density culture, the presence of weeds, insects or mechanical damage to the orchard or during harvesting, storage and distribution that can weaken the natural defense mechanisms of plants and encourage colonization by mycotoxin-producing fungi and, in turn, the formation thereof.[1,14] Then they will present the most common mycotoxins that cause harm in humans.

Aflatoxin: They are colorless, tasteless, and clarified as chemistry, they are solid in food and can cause resistance to normal processes boils, the most difficult to remove once they occur.[15] Moreover, the fungus *Aspergillus* flavus factory mycotoxins called aflatoxins B1, B2, while the fungus *Aspergillus* parasiticus produce mycotoxins known as aflatoxins B1, B2, G1, G2. All being potent carcinogens.[16] Of these, aflatoxin B1 is considered natural carcinogen, because its toxic mechanism is mediated by the epoxide radical which interacts with fusion proteins, causing toxicity and prevent protein synthesis and immunosuppression, similarly, it is able cause genotoxicity and induce carcinogenic processes, M1 and M2 aflatoxins are metabolic derivatives of aflatoxins B1 and B2, which are eliminated through urine and milk of people who have consumed contaminated feed.[17] These mycotoxins induce a variety of toxic effects on living organisms exposed to contaminated food.[18] Aflatoxins once ingested are to absorb through the gastrointestinal tract, where there will remain 36 minutes, accompanied by a volume of distribution of 14% of body weight, according to the literature about 80% of the total amount of AFB1 was eliminates AFM1 7 days and removed in the following ingestion two days, ie it constitutes 1-4% of the ingested AFB1.[19] Similarly they are staying in different metabolically active cells of the intestinal mucosa, mainly in the liver, where there suffer a biotransformation process through mechanisms epoxidation, hydroxylation, methylation or des, conjugation and spontaneous processes.[20] Tests in animals have indicated that aflatoxins cause acute and chronic toxicity. Acute effects include liver death, nephritis, and pulmonary congestion. Chronic effects include cell damage, carcinogenicity, mutagenicity and teratogenicity in animal models.[21] As for carcinogenicity of aflatoxins, according to the literature is the microsomal P450 biotransformation AFB1-8,9-epoxide hepatic system, this is capable of binding proteins, to deoxyribonucleic acid and ribonucleic; to determine a solid compound with guanine residues and does cause mutations in codon 249 of p53 tumor suppressor,[22] also this alteration is characteristic of various carcinomas, particularly hepatic carcinoma in man.[9]

Ochratoxin A (OTA): It is a solid, colorless and easy mycotoxin dissolve polar organic compounds. However it is very soluble in water, with characteristics of weak acid and capable of expressing fluorescence when stimulated with ultraviolet light[23] is considered neurotoxic .Igualmente because They are capable of causing adverse effects on the central nervous system, the peripheral nervous system and organs, Immunosuppressant that weakens the immune system, genotoxic and making changes in the transformation of cells causing malignant tumor DNA, made carcinogenic and teratogenic cause cancer because crosses the placental barrier causing damage to the fetus.[24] Ochratoxin A once been absorbed by the gastrointestinal tract passes into systemic circulation, where there can be detected in tissues and blood. Ie, higher concentrations are detected in the most metabolically active organs such as liver, kidney, muscle and fat.[23] Moreover, during distribution, ochratoxin A has higher affinity for adaptation to plasma proteins, presented a half-life of prolonged excretion, ie in man of 840 hours (35 days), the free toxin dose <0.2%[23] and excrete their waste by renal and hepatobiliary[25] route. On the other hand, pollutes human foods such as cereals, wheat, barley, corn, rice, grapes, wheat flour, cornmeal, oatmeal, bread, and derivatives, alcoholic beverages, such as red wines, wines pink, white wines, beer with alcohol, non-alcoholic beers, stouts and milling products (coffee, cocoa).[26] Likewise, the values of ochratoxin A in foods are intertwined with processing environments and maintenance.[27] That is, if agricultural practices and environmental conditions (humidity and temperature) during storage and shipping are not adequately performed, it will favor the production of ochratoxin A in these foods.[28] This mycotoxin acts altering the cell oxygen.[29–32]

Patulin: It is a mycotoxin mainly penetrates products apple as juices, juice or cider, because it is highly soluble solid in aqueous media, and can withstand thermal processing juices pasteurizados10;[10] produces toxic effects as genotoxicity, immunotoxicity and neurotoxicity in humans and animals in the body causing effects as weakening of the immune system and the nervous system aggression.[24] At the cellular level it has been shown that Patulin causes various toxic effects, including disturbance of the plasma membrane, where there is an impairment of synthesis accompanied protein transport inhibition amino acid linked with Na+, according to the literature via disorder transcription and translation and inhibition of DNA synthesis .[5]

Deoxynivalenol (DON): They are produced by fungi of the genus phytotoxic Fusarium1. These mycotoxins are common contaminants of cereals such as wheat, corn, barley and silage. Toxic symptoms attributed to deoxynivalenol are associated with nausea (vomiting), food refusal, gastroenteritis, diarrhea, immunosuppression and hematological disorders.[13] The mycotoxin Deoxynivalenol through the intestinal mucosa through the tight junctions. At the same time, it increases the permeability for Deoxynivalenol intestinal cell by opening the tight junctions, causing this mycotoxin is moved by circulation to other organs leaving toxin and thus produce pathology.[33] In addition, allowing a larger number of bacteria can move through the intestinal epithelium,

Mycotoxins detection methods

The determination of mycotoxins is not so simple, because they are dispersed heterogeneously in the food. Analysis can be divided into four phases: first obtaining a representative sample of the batch, the second grinding said sample is performed, the third extraction for removal of mycotoxins insoluble compounds in the solvent extraction is done and finally the clean-up phase which are separating mycotoxins other accompanying substances in the extract is effected, this is accomplished by pre-packed with silica gel, florisil or ion exchange columns; also by liquid-liquid extraction and immunoaffinity columns thereby obtaining optimal and reliable concentration of mycotoxins.[34]

For determining them, various types of methods which detect the different mycotoxins in contaminated food, among the most common are used:

a. **Columns quantitative luminescence method:** is a quantitative method for the detection of mycotoxins in many products, such as ground cereal, rice, corn, fruit between others.28 also is a test used in a wide variety of places or farms food processing and laboratory quality control it is quick and easy to interpret.[35]

b. **Direct competitive ELISA method:**is a competitive enzyme immunoassay is based on antigen-antibody reaction, it is used for quantitative analysis of mycotoxins mainly in foods like corn, wheat, barley, oats, peanuts and fruit. It is more effective, because giving reliable and accurate results.[36,37]

c. **Layer chromatography** fine: It is an analytical technique widely used in the laboratory for the detection of mycotoxins, which determines the degree of purity of the mycotoxin, compare samples and track a reaction.[38]

d. **Liquid chromatography**: It is a high throughput technique that is used in the fields of biochemistry to separate and identify compounds based on their polarity. The device employs a pump acting to create a pressure high enough to force the compound to be separated into polarized through the device[39] particles.

In this table we will present the advantages and disadvantages of detection methods for mycotoxins (Table 1).

Table 1 Advantages and disadvantages of detection methods for mycotoxins

Method	Advantages	Disadvantages
Direct competitive ELISA method[47]	simplicity: Reagents used in small volumes and the separation of free and bound reagents is made by a simple washing procedure	The ELISA test can be developed in laboratories of low complexity, being less expensive than chromatographic technique.
	Reading: The final colored product can be read with the naked eye to evaluate how it has been worked test	
	Speed: The test may develop within hours. The spectrophotometric reading of the results is fast	
	Sensitivity: Detection levels of 0.01 to 1.0 ug / ml, ideal for most diagnostic	
Liquid chromatography and Layer chromatography fine[48]	HPLC is an automatic process that takes only a few minutes to produce results. This is a marked difference in liquid chromatography using gravity rather than a high speed pump to force compounds through a densely packed tube. The results are high resolution and easy to read, and tests reproduce easily through the automated process	It is difficult to detect coelution (two compounds escaping from the pipe at a time) with HPLC, which can give incorrect categorization compound. There is a high cost to the need to carry out HPLC equipment. Its operation can be complex and requires a trained technician to operate. Because the process speed, the equipment has low sensitivity to certain compounds

Discussion

According to the results obtained in the literature review, mycotoxins generate effects in humans due to the consumption of food contaminated by fungi of the genus *Aspergillus* spp, Penicillium spp and Fusarium spp, causing diseases affecting organs like kidneys, liver and muscle. The presence of these mycotoxigenic fungi and their toxins production is a major public health problem, being more frequently than aflatoxins develop liver cancer and kidney failure; ochratoxin with patulin producing nephrotoxicity, immunosuppression, genotoxicity, and finally teratoxicidad deoxynivalenol generating immunosuppression and haematological disorders.[7,9,22] Currently mycotoxin analysis presents several challenges that have not yet found a definitive solution. Thus one of the problems of great interest that affects the consumer today is the presence of mycotoxins in foods such as cereals and their derivatives, apple, pear, grapes, alcoholic drinks, coffee, cocoa, milk, meat, eggs and nuts.[40] To prevent (but not eliminate) this contamination is essential to proper management of crops, in the steps of the processes and control silages conditions which are developed; They are the preventive measures to reduce food contamination by these mycotoxins[40] measures.

In Brazil, Diaz et al.,[41] conducted a study on aflatoxins found in foods such as corn, peanuts and beans, estimated 35% of cancer cases caused by these contaminated food. For this study 40 samples (corn, peanuts and beans) found in the central distribution Curitiba were used. Samples were identified by Kits Envirologix, and confirmed by thin layer chromatography of silicagel-G, resulting in the presence of *Aspergillus* in 60% of the samples and 35% of aflatoxin B1 and B2.

In a study by Santillán et al.,[42] reported consuming contaminated with aflatoxins that occurred in India in the 1970s, where the intake of contaminated corn caused poisoning and killing at least 97 personas41 food. Also, this study mentions a report of the most recent, in 2004, where maize contaminated with aflatoxins caused one of the biggest

outbreaks of aflatoxicosis in Kenya, obtaining as a result 317 cases of poisoning and 125 deaths. According to the studies outlined above it should be noted that the diseases caused by various types of mycotoxins are an alarm for the community, because these mycotoxins are found in most foods consumed by humans. That is why you need to implement preventive measures, such as implementing protocols that help the manufacturing process food more susceptible to contamination is appropriate, and achieve mitigate the risk of transmission.

Furthermore, it is necessary to consider the methods used for the diagnosis of mycotoxins in the laboratory, using immunochemical assays as Elisa, columns luminescence liquid layer chromatography and gas chromatography. In a study by Rojas.[43] the effectiveness of different kits Elisas and columns immunopurification where both techniques yielded optimal results with a maximum variation coefficient of 8.3% and minimum coefficient of variation of 1.9%, using more technical frequency ELISA to be less expensive and easier evaluated the other above methods.[43] This means that the ELISA is the most commonly used laboratory for the identification of these mycotoxins is used as a fast, easy and economical technique.

On the other hand, Ravelo Abreu et al.,[22] comments in his review articlecurrently the most used technique is the high resolution liquid chromatography coupled to a fluorescence detector; purification of the sample is made with cartridges containing specific antibodies (immunoaffinity columns) with the lower limits of detection are achieved and liquid chromatography coupled to mass spectrometry (LC-MS-MS) give very good results but it requires more expensive equipment and more complex.[22] According to the above, consider a remarkable example mentioned Mr. Ravelo Abreu et al.,[22] study which uses an analytical method based on the sample extraction with chloroform, the extract purification is performed by passage through immunoaffinity columns and analysis by liquid chromatography in reverse phase under gradient conditions with fluorimetric detection after post-column addition of ammonium hydroxide. However, these techniques have the drawback of being laborious and expensive, so are not suitable for analyzing a large number of samples.

In another study by Zheng et al.,[44] mentions that deliver quantitative immunoassays and fast results (ELISA) using antibodies sensitive which can interact with the food matrix, leading to under or overestimate the concentration of mycotoxins in some situations; This immunoassay is limited to mainly detect cereals, milk, cheese and nuts. According Krska et al.,[45] The LC-MS (liquid chromatography mass spectrometry) method is widely developed because of its great potential to investigate large numbers of samples and observe the presence of a large number of mycotoxins.

All previously mentioned methods have their advantages and disadvantages: Chromatographic methods provide complete and reliable profiles pollution but are expensive analysis while immunoassays test are quick, easy and inexpensive methods that can only be used for some ingredients. Selection of the proper method should be done considering the purpose of analysis, the characteristics of the sample and environmental conditions. Still, the quality of sampling is often the most critical for reliable results.[46] According to developed in this review, further progress is needed in investigations related to the presence of mycotoxins in food for human consumption, especially in tropical regions, because the environmental conditions and characteristics of the food produced in those regions favor, at least theoretically, the development of these toxins , which represents a high risk for health and food security of populations.[47–50]

Conclusion

Mycotoxins represent a danger for both human and animal health. The risks associated with health have often been characterized however have not yet defined the mechanisms by which these toxins come cause such damage. Diffusion capacity and pollution and the effects that although small doses can cause, makes them stand as a silent enemy which we must learn how to cope. The main weapon to combat mycotoxins constitutes the objective dissemination of information to all members of the food supply chains and consequent prevention and control measures that can be applied over it. Moreover must achieve unify criteria for the standardization of procedures for sampling, testing for permissible levels and trying to globalize the problem of mycotoxins and actions to counter it.

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Conflicts of interest

The authors report that in the present investigation no conflicts of interest.

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