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Current approaches regarding analysis and assessment of risks associated with aflatoxin contamination: Review

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Abstract

In the view of fulfilling the general goal of achieving a high level of protection of human life and health, food law regarding food safety is based on risk management and risk analysis, except for the cases when the situation is not appropriate to the circumstances. Safety management can be realised by using various different approaches. The lack, at global level, of precise and coherent information regarding chemical contaminants and the toxins existent in the food chain gave an exact epidemiologic estimate exactly in regards to the food poisonings caused by the contaminants in food products. Taking into consideration that the intrinsic toxicological properties of chemical substances cannot be changed, the political regulations are often compromised by the analytical detection limits, and/or even by the commercial relations between countries. Even though laws in more countries have established official methods for detecting a great number of food contaminants, there are a lot of contaminants still developing, that are not yet taken into consideration.

Keywords: aflatoxin, hazard identification, hazard characterization, exposure assessment

1.Risk factor analysis

Among the general principles well-known in the area of the food law, risk analysis and the precautionary principle are a novelty, having been brought under regulation for the first time in the EU.

However, in the public context, there is an approach inclining towards the consistent use of risk-based management in a general framework, mentioned as risk analysis, and so the European Regulation defines the elements of risk analysis in the following way [1]:

"*Risk*" means a function of the probability of a negative effect on health and the severity of that effect, determined by a health hazard.

„*Risk analysis*" infers a process consisting of three interconnected components:

risk assessment - its purpose is to evaluate the risk and consists of an scientific assessment comprising four stages:

- hazard identification
- hazard characterization
- exposure assessment
- risk characterization

risk management is a process distinct from risk assessment, of weighing alternate policies by consulting the interested parties, taking into consideration risk assessment and other legitimate factors, and, if needed, selecting appropriate prevention and control options

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risk communication means the interactive exchange of information and opinions, throughout the risk analysis process, concerning hazards and risks, risk-related factors and risk perception, between risk assessors, risk managers, companies operating in the animal food sector and with a food profile, the academic community and other interested parties, including the explanation of the risk assessment findings and the basis of risk management decisions;

In practice, risk analysis is very complex, because it is very difficult to define the key factors and often they are impossible to be measured. It is a relatively new science that is multidisciplinary. While some aspects are relatively well established, for the most part of risk analysis in the early stages of development it is very likely that they can change dramatically in the coming decades [2].

In order to create confidence in the scientific basis of food regulation, risk assessments are accomplished in an independent, objective and transparent method, centered on accessible scientific information and data. The current approach in most countries is to use a decision-making framework for risk analysis, similar to that proposed by [3]. This approach considers scientific principles as a point of connection to human and animal health, and it includes a comparison with other risks and socio-economic factors.

Depending on the severity of exposure and the severity of disease, in particular regarding cancer, the occurrence of mycotoxins, currently, can present a higher risk than antropogens contaminants, pesticides and food additives. This is based on a comparison of potential tumours and exposure to mycotoxins [4], so that considerable international efforts have been taken to in the purpose of health risk assessment at some mycotoxins.

At the beginning of 1980, new mycotoxins have been discovered and characterized and in the case of other important mycotoxins, new data appeared regarding the determination methods, toxicological and epidemiological data on mycotoxin contamination, which led to further evaluation and updating of data and scientific evaluations by IARC and by other national agencies [5-9].

The purpose of risk analyses have as results the achievement of practical solutions that bring into balance health protection and economic concerns, therefore scientific evaluation is directed towards the international recommendations for mycotoxins (aflatoxins, ochratoxins, patulin, zearalenone and fumonisin) of the Codex Alimentarius Committee on Food Additives and contaminants (CCFAC) and the European Union.

1.2.Analysis probability. A great part of the risk analysis means assessment, quantification and expression of probabilities. Experience regarding many contaminants is very limited, because the specific elements of human metabolism and toxicity are poorly understood, and the best existing models are animals, as in their case biological characteristics may resemble those of humans. Real exposure levels cannot be determined at a true value, as well as the unpredictability of interactions with other chemicals, both natural and synthetic.

Costs and benefits associated with food contaminants are hard to quantify and the needs, views and expectations of the interested parties are difficult to assess. In the absence of such knowledge, conservative assumptions are used most often [2].

2.Risk assessment

Risk assessment is the component based on the science of risk analysis that characterizes the probability of exposure to risk, as well as the consequences of exposure for the consumer.

It is a set of logical, systematic activities, based on analytical evidence designed to obtain an understanding of the specific risks, and to measure and describe to the greatest extent possible. A risk assessment aims to answer questions, the risk manager should know about the identified risks and provides objective information necessary for decision making.

In the case of contaminants, risk assessment rarely ends by probable estimation of risks of adverse effects that may occur in a defined time interval. Sometimes it is possible to perform probable estimates of risk, but even here the risk assessment tends to be expressed in terms of risk exposure, which often means and acceptable risk (eg. out of a million, one individual may be affected) [2].

Nevertheless an approach "margin of exposure" was developed for substances that are both genotoxic and carcinogenic, which is now used by the World Health Organization and by the European Food Safety Authority [10].

2.1.Principles of risk assessment. The most important principles underlying a good risk assessment include: a systematic, structured, objective and transparent approach, providing relevant documentation in order to allow InterPARES evaluation on communication for various interested parts, ensuring that the responsibilities of risk assessors and risk managers are differentiated.

A good risk assessment gives the information to the manager, and he/she treats available evidence impartially, and clearly connects the evidence with his/her conclusions [11].

A "*qualitative"* assessment of the risks is incomplete because it lacks risk calculations for negative consequences. Possible benefits of quantitative risk assessment is that sensitive risk variables influence the strongest so that they can be identified and used for establishing the priorities for a research program that could supplement the lack of essential data.

Although a qualitative quantification of risk would not include such an analysis of sensitivity, a systematic discussion and directing of hazards and risks can provide useful and reasonable understanding of "approximate" variables that could influence a further study [12].

A change suggested by the Codex Committee on Food Hygiene [13], requires replacement of the "dose-response assessment" with "Hazard characterization", a more general term that emphasizes the value of a qualitative approach when the dose-response for contaminant does not exist in populations at risk.

These changes were suggested, reflecting the need for greater interaction between research, and so Covello and Merkhoher [14] proposed *"hazard identification"* to be a preliminary stage before performing a risk assessment, rather than it being the first step in performing a risk assessment.

Selecting the managerial framework for structuring the risk assessment process is not valid or invalid to the process. What is of greater importance is the fact that the analysis is based on the best scientific knowledge available and that the key principles and guidelines are respected, so that the Codex Committee on Food Hygiene [15] chose not to provide a formula for performing a risk assessment.

The first task of risk assessors, given as one of their assignments is to carry out a risk assessment of their risk managers, is to compile samples and to structure in a reasonable manner, in accordance with a logical framework, such as the Four-Element Framework [16].

This framework is general enough to be useful for chemical and microbial hazards [17]. Therefore, producing a risk assessment is to estimate the probability and severity of negative outcomes for scenarios, depending on the alteration of Kaplan's definition of the risk [12].

2.2.Hazard identification. Hazard identification is primarily a qualitative process that describes the combination of hazards in food. The stage of hazard identification is an opportunity for risk assessors to bring to the attention of risk managers the hazards that could be considered. Each risk assessment begins with hazard identification, but identification of hazards should not lead to additional measures in assessing risks. The first step in a risk assessment process is identifying hazards, and this identifies agents that may have adverse health effects and may be present in a particular food or food groups. In this sense epidemiological information and specialty knowledge are used in order to establish connections regarding potential hazards that cause disease among consumers. For example, a chemical product which produces toxic effects shortly after ingestion in small quantities can easily be identified as a threat. However adverse health effects in the long term may be difficult to determine. This is especially a problem for chemical contaminants that may cause adverse health effects, such as cancer, after exposure at low levels on long term [11].

2.3.Exposure assessment. It is the second element that focuses on modelling hazard occurrence and hazard level, as well as the potential ingestion of toxic agents from food products, which causes or contributes to negative outcomes. Exposure

assessment usually includes an assessment of a hazard in a particular food product for scenarios that describe production, processing, distribution and preparation of food [12].

The interested parties should be aware that many technical assumptions of risk assessment are based on very limited data. Since much of the information is not known with certainty, simplifying assumptions could often lead to an overestimate of result confidence. For example, the major distinctive feature of microbial pathogens is modelling to account for the evolution of microbial growth and decline, called microbiological prediction. In the case of chemical contaminants, the main factors involved in aflatoxin exposure are examined in a global context by comparing the risk of exposure of toxins at national levels of economic and social development.

The effects that aflatoxin exposure has on human health are explored in three sections [18]:

- human diseases and nutritional status,
- carcinogenicity
- growth and development of children.

The section regarding the attenuation of the effects of aflatoxin on human health is in contrast with the efficiency of regulations regarding agriculture. In conclusion the risk of hepatocellular carcinoma in developing countries such as West Africa, may be tackled by vaccination for the hepatitis B virus. At young people in West Africa who are chronically exposed to aflatoxin in food products and consuming diets with a nutritional deficit was proved to stop growth and cause various liver diseases [19].

In developed countries, there are infrastructures for surveillance of contamination levels in food products. On the other hand, in developing countries and poor, rural, agricultural communities, exposure to aflatoxins occurs. As seen, developed countries tend to have a variety of different foods and could easily distinguish aflatoxin contaminated food or feed with other uses. For example aflatoxin contamination in corn can affect the livestock by feeding animals with those forages, if the limits set by the regulating law are not applied [18].

2.4.Hazard characterization. This is the third element of the framework that involves modelling the relationship between the ingested dose of hazardous substance, and the probability as well as the severity of the adverse effect. A great part of the dose-response activity in assessment of chemical risks involves analyzing data from animal studies [12].

Hazard characterization describes the negative effects on health and on the consumer, from exposure to the hazard. For chemical hazards, this stage develops detailed information regarding the chemical nature and how it causes adverse health effects. When possible, this stage includes quantitative information, in the form of a dose-response relation between the concentration of hazard and the effect on consumer health, as well as probabilistic estimates of negative results. Data sources for characterizing hazards include toxicity studies on animals, on the cell line, human clinical studies and epidemiological data. For deliberately added chemicals, methods have been developed to predict the probable exposure to populations, based on the intended use of the chemical product. Other methods of short-term exposure assessment were also developed for those chemicals that present acute risks. For contaminants, monitoring data is used in combination with food consumption patterns in order to estimate exposure. The connection between the scale of exposure (dose) to a chemical agent and the severity or frequency of associated adverse health effects (response) defines the dose-response relation. This relationship is often represented as a curve, such as dose-response curve [11].

The hazard characterization stage can also be described as some biological and mathematical extrapolations of the risk assessment phase, in order to make predictions regarding characterization of hazards to humans. The inherences in this process have many uncertainties, and various approaches are needed to characterize a hazard [20].

2.5.Risk characterization. It is the fourth element of the framework that begins with the output link of models for assessing exposure and dose-response assessment (hazard characterization) to predict the frequency and severity of human disease (consequence) for research.

This element is defined as an estimate of the possibility of incidence and severity of known or possible adverse effects on the health of a population based on previous stages; it also includes results of risk assessment, in the form of risk estimates, risk descriptions.

A characterization usually includes one or more risk estimates. A risk estimate is an estimate of the probability and severity of adverse health effects, with related uncertainties.

Evaluation of risk management options requires estimating "basic" risks, understanding of the public perceptions of danger, as well as inequalities in the distribution of benefits and risks. The assessment should include the effects of risk, as well as a reduction estimate of the risk expected under alternative strategies for reduction.

Assigning a risk level represents a similar approach that can be used in the case of mycotoxins and should take into account the stage of life, as well as the groups most susceptible to exposure or vulnerability, such as infants and toddlers (for low body weight and possibly increased sensitivity), as well as for other groups that may have differences in bioavailability, such as the elderly or individuals with specific genetic predispositions.

Regarding contamination on short term, it must be considered whether the toxicity is associated with peak concentrations and chronic exposure, duration, exposure degree and mode of action, being possible to determine if the exposure can be taken into account and if it falls within permissible TDI limits [21]. So that for some substances exposure averaging can give an indication of the degree of risk.

Probabilistic methods for NOAEL and uncertainty factors are replaced by combining distribution with probabilistic exposure assessment, which can be helpful in estimating the risk distribution for different goals and different segments of population [20, 21] This approach was used in the Netherlands when they were faced with high levels of deoxynivalenol [22].

3.Risk management.

Risk management includes the information derived from the risk analysis and turns it into a political decision. The purpose of risk management is to make the decisions regarding the current global context, thus it is crucial that the social, political, and economical factors be fully taken into consideration.

Risk management and risk administration take into account the results of risk assessment and, in particular, the notifications of the Regulation Authorities and other legitimate factors regarding the matter of fungal contamination of milk and milk products, as well as the precautionary principle.

For the most important mycotoxins of economic importance (aflatoxins, ochratoxin A, fumonisin, deoxynivalenol, zearalenone and patulin), continuous monitoring is necessary, as well as risk reduction, to ensure that exposure does not pose any health risk.

Risk management presents some risk reduction priorities, and they depend mostly on the frequency and extent that TDI is exceeded, so that in risk management there are a variety of risk management options that can help ensure food safety conditions.

In recent years, the Codex Alimentarius has developed a code of practice for prevention of contamination with mycotoxin in cereals and feed [23]. Over the years most countries have established maximum residue limits for a variety of mycotoxins. At present, risk assessment became the basis for establishing the regulations concerning contamination. In this view, regulatory standards have been adopted, which reflect the level of security deemed appropriate for a particular hazard. The political strategies for better control of food-borne hazard can create new hazards [12].

4.Risk communication

Providing information to the public regarding the nature of the risks is generally viewed as the last stage of risk analysis. It is unanimously accepted that the public has the right to know how decisions about risk have achieved their purpose, and sometimes even the information that was used in the risk assessment and risk management should be made available to them. Some regulation authorities believe that the information transmitted to the public should be as technical as possible, so as their decisions be more

easily accepted. The Codex Alimentarius definition of risk management recognizes that the information needs to flow in a two-way direction, between consumers and the regulators. However, the subject that the consumers should be a part of the decision making process is highly debated [2].

5.Conclusion

Adopting risk analysis in the domain of food safety could offer governments a strong tool for assessment and management of the risks created by potential hazards in food products. This approach may offer a logical context for making complex decisions regarding public health, in an economical and social context.

At the same time, risk analysis may encourage a better interactive communication between all the parts that are involved, and it has also been recognised, on global level, by health and commercial organisations as a basis for establishing the health and safety requirements for food products. As a consequence, the food safety authorities at international, national and local level should make big efforts in order to understand and apply the risk analysis principles and procedures, particularly those used by international organisations

Hazard identification, exposure assessment, hazard characterization and risk characterization could allow the development of decision-making tools for assessment of the quantitative risk, namely the separation of scientific / technical factors that create risks for consumers. This tool could be applied in all stages of the food chain. In addition, this tool can consider a risk map as a general tool for relations between different elements (exogenous and endogenous) of the chemical compounds, as they show the highest complexity mark on the overall system.

Recent studies in the field of risk assessment tackle a combination of omics technologies, biological systems and mathematical models. These techniques are used to identify the metabolic pathways leading to cell interactions, and then to disease.

Considering recent developments of omics technologies, which represent an important potential tool in assessing health risks of food products, these techniques will allow detection of RNA changes, proteins or metabolites at a level close to the actual exposure levels. Also, they could contribute significantly in understanding the combined effects of contaminants in close relation with mathematical modelling. The data generated by using these tools will allow researchers to obtain increasingly detailed images in cellular responses to changes in the environment.

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References

1. Union, E., Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, in Reg. CE. 178/2002, E. Commission, Editor. 2002, © European Union, http://eur-lex.europa.eu/, 1998-2014: Bruxelles.
2. Benford, D.J. and D.R. Tennant, *Food chemical risk assessment*, in *Food Chemical Risk Analysis*, D. Tennant, Editor. 1997, Springer US. p. 21-56.
3. FAO., *Worldwide regulations for mycotoxins in food and feed in 2003*. 2004: FAO.
4. Kuiper-Goodman, T., Food safety: Mycotoxins and phycotoxins in perspective. Mycotoxins and Phycotoxins - Developments in Chemistry, *Toxicology and Food Safety*, **1998**, 25-48.
5. Castegnaro, M., I.A.f.R.o. Cancer, and W.H. Organization, *Mycotoxins, endemic nephropathy and urinary tract tumours*. 1991: International Agency for Research on Cancer Lyon.
6. IARC, Iarc Monographs Program on the Evaluation of Carcinogenic Risks to Humans-Preamble. *Monographs on the Evaluation of Carcinogenic Risks to Humans*, **1993**. *56*, 13-32.
7. Organization, W.H., *Selected mycotoxins: ochratoxins, trichothecenes*, ergot/published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization. **1990**.

8. Marasas, W., et al., *Environmental health criteria 219: fumonisin B1*. World Health Organization, Vammala, **2000**: p. 9.
9. Kuiper-Goodman, T., P. Scott, and H. Watanabe, Risk assessment of the mycotoxin zearalenone. *Regulatory toxicology and pharmacology*, **1987**. *7*(3), 253-306.
10. Barlow, S. and J. Schlatter, Risk assessment of carcinogens in food. *Toxicology and Applied Pharmacology*, **2010**. *243*(2), 180-190.
11. L.G.M. Gorris and C Yoe, *Risk Assessment: Principles, Methods, and Applications*, in *Encyclopedia of Food Safety*, Y. Motarjemi, Editor. 2013, Elsevier Science.
12. Coleman, M.E., et al., *Risk Analysis Frameworks for Chemical and Microbial Hazards*, in *Food Safety Handbook*. 2005, John Wiley & Sons, Inc. p. 19-46.
13. Codex Committee on Food Hygiene, Principles and Guidelines for the Conduct of Microbiological Risk Assessment. **1998**. Alinorni 991 13A, Report of 3 1 st Session of CCFH.
14. Covello, V.T. and W. Merkhoher, *Risk Assessment Methods: Approaches for Assessing Health and Environmental Risks*. 1993: Springer.
15. Commission, C.a. *Report of the thirty-first session of the codex committee on food hygiene*. 1998.
16. National Research Council, *Risk assessment in the federal government: Managing the process*. 1983: National Academy Pre.
17. Marks, H.M., et al., Topics in microbial risk assessment: dynamic flow tree process. *Risk Analysis*, **1998**, *18*(3), 309-328.
18. Abbas, H.K., *Aflatoxin and food safety*. 2005: CRC Press.
19. Cardwell, K.F., S.H. Henry, and H. Abbas, Risk of exposure to and mitigation of effects of aflatoxin on human health: a West African example. *Aflatoxin and food safety,* **2005**, 213-235.
20. Edler, L., et al., Mathematical modelling and quantitative methods. Food and Chemical Toxicology, **2002**. 40(2): p. 283-326.
21. Renwick, A., et al., Risk characterisation of chemicals in food and diet. *Food and Chemical Toxicology*, **2003**, *41*(9), 1211-1271.
22. Pieters, M.N., et al., *Risk assessment of deoxynivalenol in food: concentration limits, exposure and effects*, in *Mycotoxins and Food Safety*. 2002, Springer, 235-248.
23. Commission, C.A., Proposed Draft Code of Practice for the Prevention (Reduction) of Mycotoxin Contamination in Cereals, Including Annexes on Ochratoxin A, Zearalenone, Fumonisins and Tricothecenes. Codex Committee on Food Additives and Contaminants, Thirty-fourth Session, **2002**.