Mycotoxins

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Mycotoxins are secondary metabolites produced by fungal species that commonly have a toxic effect on human and animal health. Different foodstuff can be contaminated and are considered the major source of human exposure to mycotoxins, but occupational and environmental exposure can also significantly contribute to this problem.

Keywords: mycotoxins ; biomonitoring ; human health ; exposure

1. Overview

Food safety has become an important term for authorities and consumers. The aim is to keep the consumers safe from any harmful compounds and to ensure the producers from economical losses in case of an outbreak of contaminants in the production chain. The recommendations and the measures taken by the companies and the legal bodies are based on risk evaluations reported by food safety authorities [1]. Current regulations are established on scientific opinions given by eminent institutions such as FAO/WHO Joint Expert Committee on Food Additives of the United Nations (JECFA) and the European Food Safety Authority (EFSA). This includes the involvement of AOAC International (Association of Official Analytical Chemists) and the European Standardization Committee (CEN) who are obligated to monitor and implement the requirements for adequate sampling and analytical methods [2]. The important stages of risk evaluation studies are to identify and characterize contaminants and to evaluate the exposure to certain hazardous materials [2][3][4]. This often means the implementation of long-term monitoring of the occurrence of concerning substances in food. Food contaminants consist of different compounds. The most common contaminants are mycotoxins (single or mixed) and other toxins produced by various fungal species [1], some of which belong to the genus Aspergillus, Penicillium, Fusarium, and Alternaria [5]. Mycotoxins and general exposure to their effect have become a major concern for the scientific and popular community. Mycotoxins are a big group of compounds, with a range of chemical structures and toxicological properties [6]. The most common mycotoxins included in legislation belong to several types: aflatoxins (AFs) and ochratoxins (OT'), fumonisins (FBs), trichothecenes and zearalenone (ZEA), patulin (PAT), and citrinin (CIT) [7]. The main food groups affected by fungal metabolites are different cereals, dried fruits, nuts, coffee, and spices [5]. Well-developed strategies including contamination control measures and improvements in processing technologies are efficient in mycotoxins prevention but despite these efforts, up to 80% of food still ends up contaminated by mycotoxins [8][9] and it has been estimated that cca. 25% of cereals worldwide are contaminated with mycotoxins [8]. Reduction of mycotoxins contamination via food processing (higher temperatures or high pressure) is minimal and allows them to linger in food items. Destruction in the gastrointestinal tract is also minimal. This is why they can act in such a harmful way and affect human and animal health. Their pronounced influence on the global economy is also tremendously important [10].

To regulate human exposure to food contaminants, especially mycotoxins, human biomonitoring (HBM) emerged as a recognized, efficient, and cost-effective method [11]. By applying HBM, it is possible to track exposure points and set minimum and maximum exposure limits. The research possibilities of HBM application can be used to understand the population range values and identify consumer groups and individuals or groups (e.g., geographically). This aims to detect higher exposures and also to confirm the regional and temporal variability for trends within a population [12]. To conduct valid research, several set-points regarding HBM need to be addressed. It is very important to provide a sufficiently sensitive and validated analytical method to obtain accurate measurements of a biomarker that correlates with the external dose [12]. The most commonly used biological material for HBM is urine, plasma, or blood. Urine is, however, preferred in field studies due to the noninvasive sampling method. This generally helps to gain higher acceptance by study participants [13]. The suitability of the biomarker or matrix greatly depends on the toxicokinetic profile of the studied compound. Detailed knowledge of the compounds' toxicokinetics, such as general metabolism properties and excretion timeline, is necessary to translate the existence of HBM biomarker data into daily intake estimates [12].

Exposure to mycotoxins does not always have to be related to food consumption. There are studies [14][15][16][17][18][19][20][21][22] that explored the occurrence of mycotoxins in working or living environments and the results showed that exposure to mycotoxins can be related to these places too.

2. Exposure Assessment

Exposure assessment is a difficult and synergistic approach including all available data is crucial for a sound conclusion. According to several authors, HBM, in correlation with different dietary surveys can be more useful for confirmation of exposure to mycotoxins, because it connects exposure to certain foods but it can expose the influence of other factors (differences in exposure due to socioeconomic or regional factors) to the results [23][24][25]. In short, HBM can be more of use in human health and dietary studies, than its use in exact exposure assessment of daily intake [26]. Exposure assessment of daily intake from blood or urine concentration remains difficult unless the human toxicokinetics and inter-individual differences are better understood [23][26].

2.1. Relevant Strategies for Data Collection

To assess the shifts in mycotoxins exposure, food consumption surveys are regularly updated. However, increased consumption of nutty cereals or beer may increase the exposure to mycotoxins present in nuts and cereals (malt), such as deoxynivalenol, aflatoxins, or ochratoxin A. Monitoring studies and data collections are important for analyzing trends in mycotoxin occurrence in raw materials and foods. The timely and continuous follow-up results with an updated exposure assessment, which is very important for HBM studies, and most importantly can lead to appropriate reactions and reduction recommendations. There are several methods, described below, that ensure data collection for further processing.

Food consumption surveys are conceived as questionnaires filled by volunteers who individually and in detail reminiscence at least two days of their diet. Such data sets are useful in aiming the assessment of dietary exposure to certain mycotoxin in the general population [27][28]. The major EU institution for such assessments is the European Food Safety Authority (EFSA), which formed the Comprehensive European Food Consumption Database, also called EFSA Comprehensive Database [29]. Global assessments are done by the Food and Agriculture Organisation (FAO) of the United Nations. EFSA also implemented the food classification system named FoodEx1 which serves to codify all foods and beverages present in the database. FoodEx2 is an upgraded version and enables more precise reporting of consumption patterns. These databases are holding information about food consumption pattens of infants, toddlers, children, adolescents, adults, and the elderly for the different Member States. Complex statistical methods are applied and the amount of data resulting from these surveys is vast. However, these summary statistics is a useful and quick screening tool in assessing chronic and acute exposure to hazardous substances. EFSA uses the detailed underlying consumption data at the individual level to perform more refined exposure assessments, both acute and chronic. System for Food Contamination Monitoring and Assessment Program, commonly known as GEMS (Global Environment Monitoring)/Food operated by WHO implements the program in cooperation with a network of Collaborating Centers and acknowledged worldwide national institutions. WHO and FAO have actively worked toward obtaining as much new data and have recently developed a new database for Individual Food Consumption Data which provides summary statistics at three levels of food categorization and can be used for an indication of the dietary exposure at a national level.

Data Collection

Data collection for exposure assessment can be related to several methods described in the following sections.

Food monitoring studies aim to investigate the prevalence and concentration of various contaminants, in an ingredient or food [1]. The procedure of sampling includes a random collection of samples from various points in the supply chain. An important point, is that this allows for the tracking of food products and relates this tracking back to the producer. Sampling can be done over a designated time. Samples can also be provided by surveys which are frequently published in the literature and available to the public [30][31][32][33]. For such studies, classification and description of foodstuffs play an important role in exposure estimations for the general population based on the geographical origin. This also contributes to the diversification of consumers to sensitive groups in the population (infants or people with specific diets) [34]. Important parameters such as sample size, sampling strategy, and sample preparation have to be noted as they could influence the results [35]. Immunoassays can be utilized as a screening method and can be a useful tool in assessing exposure. If not to determine the presence of a compound then to exclude its presence above a certain limit.

Total diet studies evaluate food samples which collectively make up a sample of the whole diet. Samples are collected, prepared, and pooled into composite samples per food category, as described in Ref. [36]. In such studies it is important to include seasonality because some foods may contain various mycotoxins levels due to climatic conditions). Geographical variation [37] is also important to incorporate since it covers the potential geographical differences. According to food safety authorities, EFSA, WHO, and FAO, the food list should cover about 90% of the food intake, should be as close as possible to the actual whole diet, and should include beverages and drinking water [36]. Representative food items and

food processing habits should be as close as possible to the habits of the investigated population. In a total diet-like study, the food items for which contamination levels of the relevant (group of) substances are expected are sampled separately [37].

EFSA employs two types of total diet studies [37]:

(a) total diet study for screening (limited number of composite food samples for common food categories). In the case of high exposures, further examinations are performed to identify the source.

(b) total diet study for refined exposure assessment (a large number of samples for smaller, more refined, food categories).

Duplicate diet studies aim to provide a copy of all food items and beverages as consumed by one person at a certain time, e.g., during a 24 h period. Such studies measure the actual exposure of consumers to compounds of interest, but the effects of food processing and preparation are also considered . Duplicate diet studies have various different version. For example, where only a portion of the diet is collected, or where foods are collected based on standardized or average diets [1]:

(a) cyclic sub-portion duplicate diet,

(b) subpopulation duplicate diet,

(c) targeted food duplicate diet and

(d) the total population diet.

Some of the methods for exposure assessment are described in the Dietary Assessment: A resource guide to method selection and application in low resource settings, a detailed handbook issued by the FAO in 2018 .

2.2. Exposure Assessment

Exposure assessment is defined as the qualitative and/or quantitative evaluation of the likely intake of chemical agents via food as well as exposure from other sources if relevant [1]. According to several authors, to estimate the dietary exposure of humans to mycotoxins, it is important to manage as much information on prevalence and levels in foods as possible and to combine them with consumption data [3]. Strategies employed to assess exposure can detect acute or chronic exposure.

Point estimate—a single mycotoxin concentration is combined with a single input parameter for consumption. The result is a single exposure estimation with a high degree of uncertainty. Data on concentration commonly originates from a food monitoring study or a total diet study which makes the conduct of such studies considerably facile [1].

Observed individual mean—is defined as the mean mycotoxin concentration per food product, combined with the food consumption per day per consumer, averaged over the days available in the survey and, divided by the individual’s body weight (average exposure/kg of bw/person/day).

A probabilistic approach is designated to assess acute and chronic exposure.

(a) acute exposure—can be assessed by combining daily individual consumption patterns from a food consumption survey with randomly selected levels per food product from a databank with mycotoxin levels in individual samples [1].

(b) chronic exposure—statistical models that use the same input as the observed individual mean approach (see the previous section) help in gaining exposure to the certain mycotoxin.

The positives and negatives for both methods are in detail described in [1].

Dietary exposure using duplicate diet studies conducts the analyses of the compounds, resulting in an actual exposure level per day for that individual. The collected food consumption data can be used to evaluate the possible sources of exposure. Acute exposure can be evaluated if duplicate portions are collected on one day per individual.

The heterogeneous distribution in the matrix, differences between geographical regions, climate, and processing methods can make the assessment of mycotoxins to be difficult and complicated. Low concentrations, co-occurrence, and biotransformation to modified forms also make this kind of research complicated.

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