



## Review

## Overall internal exposure to mycotoxins and their occurrence in occupational and residential settings – An overview

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## ABSTRACT

Mycotoxins are toxic secondary metabolites of various fungal species that can contaminate food and feed, as well as indoor environments. Numerous studies have summarized the adverse health effects of mycotoxins and described severe intoxications of humans and animals. The major health concerns are caused via the alimentary route which unambiguously is the main source for human internal exposure; however, the relevance of other pathways under environmental and occupational conditions should also be considered. Thus firstly, this review aims in summarizing literature data on potentially inhalable mycotoxins occurring in dusts or air in residences and in working environments. Secondly, it gives an overview of the overall internal body burden of mycotoxins in humans in an attempt to characterize total human exposure. These data are also discussed in relation to the current toxicologically based values used for risk assessment.

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**Abbreviations:**  $\alpha$ -ZAL,  $\alpha$ -zearalanol;  $\alpha$ -ZEL,  $\alpha$ -zearalenol; AFB<sub>1</sub>, aflatoxin B<sub>1</sub>; AFB<sub>2</sub>, aflatoxin B<sub>2</sub>; AFM<sub>1</sub>, aflatoxin M<sub>1</sub>;  $\beta$ -ZAL,  $\beta$ -zearalanol;  $\beta$ -ZEL,  $\beta$ -zearalenol; CIT, citrinin; DON, deoxynivalenol; ENN, enniatins; FB<sub>1</sub>, fumonisin B<sub>1</sub>; FX, fusarenon-X; LOD, limit of detection; LOQ, limit of quantification; M/P, milk-to-plasma ratio; NIV, nivalenol; OTA, ochratoxin A; OT $\alpha$ , ochratoxin  $\alpha$ ; OTB, ochratoxin B; OT $\beta$ , ochratoxin  $\beta$ ; PAT, patulin; SG, satratoxin G; SH, satratoxin H; STC, sterigmatocystin; TDI, tolerable daily intake; ZAN, zearalanone; ZEN, zearalenone.

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## 1. Introduction

Mycotoxins are harmful to human and animal health and have received substantial attention since the discovery of aflatoxins in the 1960s (Asao et al., 1963). Since that time, mycotoxin-producing fungi, their different chemical classes of secondary metabolites and their toxicological properties and associated health concerns have become a challenging issue for researchers worldwide. Individuals can be exposed to mycotoxins via the alimentary or inhalative route, or occasionally via skin or mucosa contact. Today, approximately 400 secondary fungal metabolites are known to be mycotoxins, possessing carcinogenic, cytotoxic, neurotoxic, tremorgenic, immunosuppressive, estrogenic, teratogenic, hepatotoxic, and nephrotoxic effects. Amongst others, *Aspergillus*, *Penicillium*, and *Fusarium* unambiguously belong to the most important genera of mycotoxin-producing fungi in food and feed (Bennett and Klich, 2003). As a consequence of ingestion of contaminated food regulations to limit the exposure of the general population have been in place for decades in approximately 100 countries (Van Egmond et al., 2007). Important mycotoxins regulated in food and feed by legislation of the EU are listed in Table 1.

In the late 1980s, mycotoxins were also recognized as being relevant to environmental and occupational health. Croft et al. (1986) reported one of the first cases of airborne trichothecene toxicosis in a moldy indoor environment. The symptoms resembled stachybotryotoxicosis originally known from horses exposed to moldy straw. Since then, mycotoxins and air contamination have become an integral part of research and are regularly addressed in relevant scientific congresses and journals. The first scientific conference on inhalative mycotoxin exposure and consequences for individuals took place in 1994 in New York, USA (Johanning and Yang, 1995). Afterwards, this conference topic became part of the German Mycotoxin Workshop in 1996 (Gareis and Scheuer, 1996). People living or working in water-damaged buildings, archives, cereal storage facilities, farms, composting plants, as well as modern office buildings equipped with ventilation/air conditioning (HVAC) systems can be exposed to mycotoxins via the inhalative route (Fischer and Dott, 2003; Nielsen, 2003; Jarvis and Miller, 2005). This can be a result of any (unknown) mold growth in the indoor living or working environment (e.g., on wallpapers, gypsum boards, carpets or other bulk materials, as well as in HVAC systems) or of handling mycotoxin-containing food, feed or waste. Depending on the substrates, growth conditions (e.g., temperature, pH, water activity), and properties of the fungal species, the spectrum of molds and mycotoxins that can possibly become airborne is very broad. Indoor exposure usually includes metabolites of *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*, or *Stachybotrys* species (Johanning et al., 1996; Andersson et al., 1997; Nielsen et al., 1998; Richard et al., 1999; Vesper et al., 2000; Skaug et al., 2001a; Gottschalk et al.,

2006; Peitzsch et al., 2012). Particularly in sensitized individuals already a small quantity of inhaled spores, fungal fragments, mycotoxins or other microbial metabolites can lead to allergies (e.g., asthma, allergic rhinosinusitis, hypersensitivity pneumonia), and to headache, nausea, fatigue, arthritis and other unspecific symptoms (Redlich et al., 1997; Burge, 2004; Horner et al., 1995). The acute inhalative exposure to *Stachybotrys chartarum* toxins in indoor environments in Cleveland, Ohio, resulted in severe cases of pulmonary hemosiderosis in infants (Dearborn et al., 1999) which can likely be regarded as index cases for the ongoing research and discussion of indoor mold growth and related hazards (Jarvis and Miller, 2005). Nevertheless, CDC concluded that a possible association between acute pulmonary hemorrhage/hemosiderosis in infants and exposure to molds, specifically *Stachybotrys atra*, was not proven (CDC, 2000). Thrasher et al. (2012) described severe health effects in a family occupying a water-damaged building. Here, mycotoxin testing in indoor environments has been connected with human biomonitoring.

Regarding exposure of workers in farms or composting plants, *Fusarium* toxins (which are produced pre-harvest in the field) as well as certain *Aspergillus*, *Penicillium*, and *Stachybotrys* toxins are of importance. They are primarily produced during unsuitable, wet storage conditions and have been shown to occur in respirable dusts (Hintikka, 1978; Sorenson et al., 1984; Fischer et al., 1999; Mayer et al., 2007; Lanier et al., 2012).

In addition to the aforementioned EC-regulated mycotoxins listed in Table 1, important, not regulated fungal metabolites and basic toxic properties are provided in Table 2. Other less frequently examined metabolites that can occur in bioaerosols are the fumigaclavines, tryptacidin, and tryptotoquinoline produced by *Aspergillus fumigatus* (Fischer et al., 1999), kojic acid produced by *Aspergillus flavus*/*Aspergillus oryzae*, and meleagrins produced by *Penicillium brevicompactum* (Fischer et al., 2000). These compounds will likely receive more attention in the future when being regularly measured (Täubel et al., 2011). There is little information in literature regarding the secondary fungal metabolites of the very frequently occurring *Cladosporium* (C.) spp. Cladosporin, produced from *Cladosporium cladosporioides* and also known as asperentin, acts as a growth inhibitor against fungi; however, its effects on mammals are unknown (Wang et al., 2013). *Alternaria* spp. are commonly found on indoor materials, but little is known about the occurrence of their toxins in bulk samples, air, or dust. Ren et al. (1998) showed that at least two of the *Alternaria* toxins, alternariol and alternariol methyl ether, could be produced on artificially inoculated ceiling tiles. Recently, alternariol, alternariol methyl ether, and altenuene were measured in building materials and indoor dust samples in a study from Finland (Täubel et al., 2011). Additionally, beauvericin, certain enniatins and other less-studied metabolites were demonstrated to be indoor contaminants using multi-analyte methods.

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