

OCCURRENCE OF MYCOTOXINS IN INDOOR ENVIRONMENTS

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SUMMARY

We present here the current knowledge on the occurrence of mycotoxins in indoor environments, considering residential homes, schools, offices, and other public buildings. Studies from close to three decades that report on the detection of mycotoxins and fungal secondary metabolites in actual indoor sample materials have been reviewed.

Research on indoor mycotoxins has almost exclusively been conducted in the context of dampness and mould contamination in buildings. There is a striking lack of studies that would target a large variety of mycotoxins in samples collected from indoor environments with and without moisture damage. The absence of comprehensive index/reference data impedes attempts to conclude on the most relevant indoor mycotoxins associated with observations of indoor moisture problems. Epidemiological studies to clarify potential health effects of indoor mycotoxins are still scarce.

INTRODUCTION AND SCOPE

This overview of the literature on occurrence of mycotoxins in indoor environments has been carried out as a contribution to the book "Environmental Mycology in Public Health" that is expected to be published in September 2015 (Academic Press, Elsevier). Here, we present the main findings of this review and propose the future challenges.

We have considered studies that report on the actual indoor occurrence of mycotoxins and other fungal secondary metabolites, i.e. studies that report the detection of such compounds in naturally infested indoor sample materials; we restricted the review to non-occupational settings. Mycotoxin production under laboratory conditions by fungal strains that may or may not have been collected from indoor environmental samples is not discussed in detail here. There is a variety of factors that might impact on the production of secondary metabolites, such as the availability of nutrients and growth substrate on indoor surfaces, water availability, temperature and other environmental factors (1-3), as well as species succession and interaction with other microbes present. Thus, mycotoxin production of a given fungal strain under laboratory conditions does not imply that any of the same mycotoxins are necessarily produced by this fungus under 'real life conditions' in a building.

'Mycotoxins' per definition are fungal secondary metabolites that pose a potential health risk to humans and/or animals when introduced by a natural route (4). Secondary metabolites are thought to be important mediators in competitive interaction between (micro)organisms and to improve survival fitness of the producing species (5). Several hundreds of different mycotoxins have been identified and characterized so far (6), but it is estimated that tens- to hundreds of thousands unique mycotoxins are present in the environment (7). Most of these compounds have been characterized in the context of contamination of agricultural crops and ingestion exposure. However, also the occurrence of mycotoxins in indoor environments is well established (see in the following) and

inhalation exposure must be assumed. Mycotoxins are non-volatile, low molecular weight natural products that are typically chemically very stable. Even though not volatile these compounds do get airborne attached to spores, microbial fragments and particulate matter, which is relevant when considering inhalation exposure in indoor environments.

MAIN FINDINGS AND FUTURE CHALLENGES

Following the first clear postulation of a potential involvement of mycotoxins in building dampness related illness in 1986 in a Chicago home (8) and several further reports in the late 1990s on the 'toxic black mould' *Stachybotrys chartarum* and its partly highly toxic secondary metabolites (9-13), mycotoxins produced by *Stachybotrys* strains, such as satratoxins, roridins, verrucarins and spirocyclic drimanes, became the major target of research on indoor mycotoxins for almost two decades. Studies during that time typically focused on a few, specific target analytes that were mostly selected based on their toxicological relevance and suggested adverse effects on human health. Only more recently, analytical methods have been developed and applied to detect multiple different mycotoxins in indoor samples, rather than only a few specific target compounds (e.g. 14-16).

Backed up by a list of 30 studies published between 1986 and 2013 (8,11,13-40), it is evident that mycotoxins and other secondary metabolites do occur in indoor environments. Most commonly, building materials (15 studies) and dust samples (17 studies) have been collected for analyses of mycotoxins; air samples are considered less frequently (4 studies), as active air sampling is cumbersome and concentrations of mycotoxins in air in non-occupational settings are usually very low, requiring very sensitive analytical methodologies. Concentrations reported for various different mycotoxins in building material samples are typically in the order of magnitude of ng-µg per g building material (range pg/g to mg/g), or ng-µg per cm² sampled surface. Typical concentrations in floor dust or settled dust are in the range of ng/g (can reach up to µg/g), or pg per cm² sampled surface for settled dust. Reports of mycotoxins from indoor air are in the range of sub-ng/m³ to low ng/m³ of actively collected air (15,27,28,31).

Mycotoxin occurrence indoors has been almost exclusively considered in the context of dampness and mould contamination; the sample collection is typically on buildings (and materials) with severe moisture damage and/or known mould contamination. The general assumption is that moisture and mould indoors relate to excess microbial proliferation which also increases the occurrence of mycotoxins. While such assumption is comprehensible, fungi occur indoors also in absence of moisture problems. Only few studies have been conducted in a way that would allow comparing mycotoxin occurrence and levels in non-damaged control environments to moisture damaged premises (14,27-28,41-42); even less such studies have performed sample collection with sufficient sample numbers (37,40). As a result, we have very limited knowledge on which fungal secondary metabolites occur in non-damaged indoor environments and at what levels, i.e. what could be considered a normal background. Thus, it is not possible at this point to present a final conclusion on the most important mycotoxins or fungal secondary metabolites regarding their indoor occurrence. There is need for epidemiological studies on mycotoxins in different climatic regions allowing for an index/reference comparison.

More recent studies indicate that not only mycotoxins produced on indoor surfaces or in building structures are relevant for indoor exposure to mycotoxins, but that also outdoor sources need to be considered and may be relevant (35,37,40). Some plants produce secondary metabolites that are identical to fungal compounds, for example emodin or physcion. Indoor contamination by dust, soil particles and plant material from outdoors

may be source for low levels of indoor mycotoxins. It appears, that just as microbes are everywhere in our living environment, so are their metabolites.

Despite some 30 years of research on indoor mycotoxins, sound information on actual health effects is limited. Several studies present some information on health complaints or sometimes clinical data of the occupants of these buildings (8,11,13,17,23,26,38,39), but no formal statistical analyses relating the measured mycotoxin exposure of the individuals to their health outcomes were performed in any of these studies, for various reasons. Support from epidemiological studies in clarifying potential health effects upon indoor mycotoxin exposure is almost completely absent, and the results obtained so far are inconsistent. While the studies from Cai et al. (34) and Kirjavainen et al. (40) did not observe adverse effects of mycotoxin levels on asthma symptoms or asthma development, Zock et al. (43) presented indicative findings of a significant, dose-response association of mycotoxin load in dust with upper respiratory tract symptoms in Finnish teachers.

More of such systematic, epidemiological studies will be needed to better understand and assess the potential health impact of indoor exposure to mycotoxins. Complementary, mechanistic knowledge will need to be generated from toxicological studies. Research on inhalation exposure to mycotoxins is largely lacking and most of our understanding on the toxic effects of mycotoxins is based on ingestion exposure of agriculturally relevant mycotoxins. The low levels of mycotoxins in indoor air are often used as an argument to claim absence of health relevance. However, the studies carried out by Miller et al. (44) and Rand et al. (45) have indicated that also 'real-life' exposure levels of different mycotoxins can alter the expression of inflammation related genes in mouse lungs.

Last but not least, the complexity of exposure situations with multiple exposing agents present at the same time in indoor air need to be considered. *In vitro* studies indicate synergistic effects in cellular responses when considering multiple mycotoxins and mycotoxins and other microbial compounds present at the same time (46-49).

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