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FUNGAL VOLATILE CHEMICALS IN THE AIR AND THEIR EFFECTS ON HEALTH

EVRIM OZKALE KAYA

ABSTRACT. Various mixtures of gas-phase, carbon compounds volatile organic compounds (VOCs) produced by fungi are able to diffuse through the atmosphere and soils due to their small size. Fungal VOCs may contribute to a controversial medical diagnosis called ‘sick building syndrome’ or ‘building related illness’ (BRI). Both atopic and normal people exhibit statistically significant physiological and psychological effects when exposed to the odorant compounds emitted by fungi, so it has been hypothesized that these odorants may cause or contribute to BRI. Mold odors are caused by mixtures of VOCs, low molecular mass compounds with high vapor pressure that exist in the gaseous state at room temperature. Different species and strains of filamentous fungi produce different VOC profiles. Approximately 250 VOCs have been identified from fungi where they occur as mixtures of simple hydrocarbons, heterocycles, aldehydes, ketones, alcohols, phenols, thioalcohols, thioesters and derivatives. The diverse functions of fungal VOCs can be developed for use in biotechnological applications for biofuel, biocontrol and mycofumigation. Volatiles represent a new frontier in bioprospecting, and the study of these gas-phase compounds promises the discovery of new products for human exploitation and will generate new hypotheses in fundamental biology.

1. INTRODUCTION

Due to methodological and technological constraints in the study of fungal volatiles, it has lagged behind the study of other fungal metabolites. Since there has been significant progress about the highly sensitive detection capabilities in seperation techniques such as gas chromatography-mass spectrometry (GC-MS) during the last half century, it has played a major role for detecting fungal VOC. Nowadays, MVOCs from environmental samples are mainly analysed with high-resolution gas chromatograph and mass spectrometry and identified according to their mass spectra. Another applicable detector is the flame ionisation detector The VOC profile of a given species or strain vary depending on the substrate, type of nutrients, duration of incubation and temperature and other environmental parameters [1,2]. It is often stated that MVOCs are side-products of the primary metabolism of microorganisms and that mycotoxins are end-products of the

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secondary metabolism. As nutritional imbalances and disorders (e.g. lack of primary carbon and nitrogen sources) lead to expression of the secondary metabolism, changes in the nutritional state may often promote or trigger the production of several MVOCs.

Fungal growth in damp indoor environments has been correlated with adverse impact on health what is often referred to as 'sick building syndrome' [3]. In particular, occupants of damp, moldy buildings, both residential and commercial, are at increased risks of respiratory symptoms, respiratory infections and exacerbaiton of asthma [4]. In addititon symptoms related to occupancy in moldy buildings may include fatigue, headache, dermatological sysmptoms, gastrointestinal tract problems, eproductive effects as well s rheumatologic and other immune diseases.

World Health Organization Committess on Dampness and Mould [4] concluded that evidence from the publisehed studies was insufficinet to support a causal relationship between molds and most of disease symptoms reported; however evidence was suffiecient to support an association between molds and upper respiratory tract symptoms, asthma symptoms in sensitized asthmatic persons and hypersensitivity penumonitis in susceptible persons. Moreover there was a suggestive evidence of association between molds and lower respiratory llness in otherwise healthy children.

MVOCs were produced by species or strains of fungal genera which are common in environment, such as *Absidia, Acremonium, Alternaria, Aspergillus, Botrytis, Candida, Chaetomium, Cladosporium, Coniophora, Fusarium, Paecilomyces, Penicillium, Phialophora, Poira, Rhizopus, Saccharomyces Serpula, Stachbotrys, Trichoderma, Ulocladium* and *Wallemia* (5 Korpi 2009).

On the other hand, the instruments which were compromised arrays of electronic chemical sensors with appropriate pattern recognition systems, which are called 'Electronic nose' or 'E-nose' is a promising new development in the detection of fungal volatile compounds. Sensing technology provides a qualitative assessment of the variations in mass, optical or electrical properties of the sensor material after exposure to volatile compounds. This technology yields 'electronic fingerprints' that can be detected without the need to seperate the mixture into its components. Dedicated instrumentation has been developes for medical, military, pharmaceutical and regulatory applications [6]. For example fungal VOC fingerprints can be used to noninvasively discriminate medically relevant fungi and to determine the efficacy of and buildup of fungal resistance to antifungal drugs. In the food safety industry this technology provides a means of early detection of mycotoxin producing fungi in grains, fruit and meat products [7,8].

Chemical reactions may further convert the produced MVOCs into other compounds. For example, alcohols are easily oxidised to aldehydes and further to carboxylic acids and ketones may react with hydroxyl radicals in the air to form aldehydes [9,10].

Chemical reactions may also produce MVOCs in the atmosphere; the reactions between ozone (and other oxidants) and unsaturated hydrocarbons (isoprenes/ terpenes) have recently been investigated experimentally. The main products in these reactions are aldehydes, ketones and organic acids but the intermediate products formed during the reactions have been suggested to be much more irritating that the corresponding original reactants and end- products [11,12]. Finally it must not be overlooked that MVOCs may also have other sources in the environment such as building materials, human activities, traffic, foodstuffs and smoking [12].

2. Cytotoxic Activities And Carcinogenicity

The cytotoxicity of several microbial VOCs administered in fluid form directly into the culture media was evaluated in tissue culture assays, and concentrations of 1-octen-3-ol as low as 0.6 mM were found to be toxic [2].The cytotoxicity of 13 so-called MVOCs, including 1-octen3-ol, 3-octanol, 3-methyl-1-butanol, 2-methyl-1-propanol, 3- octanone, 2-heptanone, and 2-hexanone, were studied using a human lung carcinoma epithelial cell line A549 in a colony formation assay and two colorimetric assays. 1-Octen-3-ol and 3-octanol were approximately 10–100 times more cytotoxic than the other MVOCs. However, all tested MVOCs were more than 1,000-fold less toxic than the known cytotoxic substance gliotoxin measured as the concentration resulting in 50% inhibition of colony growth or absorbance [13].

In the broader list of identified MVOCs, some substances (such as formaldehyde) are classified as human carcinogens or as possible human carcinogens (such as acetaldehyde, ethylbenzene, isoprene, and styrene). Considering the low concentrations encountered in the MVOC context, cancer is not likely to be a concern.

3. Measurement And Analysis

As there are no standards, consensus, or even recommendations regarding the sampling and analysis of MVOCs, the methodology presented in the literature varies greatly and comparative data on different methods are scarce. MVOCs can be collected from ambient air with either active or passive sorbent sampling. Several sorbents or their combinations, like activated charcoal (e.g. Anasorb®747), graphitised carbon blacks (e.g. Carbotrap C, Carbopack B), silica gels (e.g. Porasil C), and polymers (e.g. Tenax®TA or GR, Anasorb®727, Chromosorb 102, XAD-4) have been used for both sampling techniques in several indoor environments [14-19]. In addition, carbonyl compounds have been collected separately with 2,4-dinitrophenylhydrazinesilica Sep-Pak®cartridges in some cases [20,21]. Tenax®TA has been widely used because of favourable properties regarding recovery, breakthrough, and precision during sampling and analysis [16]. On the other hand, activated charcoal enables longer sampling periods and the collection of very volatile MVOCs [22].

4. Exposure And Toxicity

Because of overlapping concentrations of both individual compounds and the sum of selected MVOCs in problem and reference buildings, also, the lack of standardised and validated analytical methods for MVOCs it is difficult to recognise problem buildings on the basis of MVOC measurements, or to establish reference values for MVOCs, though some suggestions have recently been presented. However, according to Lorenz et al. [23], the detection of main indicators (i.e. 3-methylfuran, 1-octen-3-ol, and dimethyl disulphide) at concentrations above 0.05$\mu g/m^3$ would clearly indicate a microbial source. In addition, the presence of at least one of the main indicators and the sum of eight MVOCs exceeding 0.6 $\mu g/m^3$ or 1.0 $\mu g/m^3$ would indicate a probable or very probable microbial source, respectively.

In a laboratory study, typical VOCs in composts included carbonyl derivatives, organosulphur compounds, pyrazines, pyridines, and oxygenated monoterpenes. Concentrations of organic sulphur compounds (thioethers, disulphides, and trisulphides) in garden waste were concluded to be sufficiently high (10–50 mg/m^3) to cause irritation and other symptoms of toxicity among waste-handling personnel [24]. Herr et al. [25] reported gradually decreasing concentrations of 11 MVOCs (in the range 0.005–6.0 μg/m^3) measured at different distances (200–550 m) from a large-scale composting site. The authors demonstrated an association between concentrations of residential bioaerosol pollution including MVOCs. To conclude, reported individual and total MVOC levels are quite low and barely exceed 1 mg/m^3, even in fairly contaminated areas.

Wolkoff et al. [26] have recently proposed that it is possible to distinguish between four types of different organic compounds in the indoor environment that could provoke sensory irritation in the airways. The groups of the proposed compounds are as follows: (a) chemically non-reactive, stable organic compounds (i.e. octane, toluene, butanol, and alike); (b) chemically reactive organic compounds like alkenes that react with ozone alone or with nitrogen dioxide in the presence of light to produce new oxygenated products; (c) organic compounds that form chemical bonds to receptor sites in the mucous membranes; and (d) organic compounds with (known) toxic properties these compounds are characterised by effects developed over long duration of exposure.

Sensory irritation is a known effect of exposure to VOCs; this effect thus also applies to MVOCs. Irritation of the eyes and upper airways (i.e. sensory irritation, also called pungent sensation), is because of stimulation of the trigeminal nerve [27]. It has been suggested that the strength of the response depends on the number of occupied receptors. Only limited knowledge exists about such receptors [28,29,26], which have been identified only in a few cases [29]. It has also been proposed that the magnitude of the response in turn depends on the chemical structure of the compounds [27]. Even small differences in the chemical structure, such as different enantiomers of the same compounds, may affect the potency [30,31].

5. Conclusions

However, among the compounds identified so far, none has been verified as a 'pure', MVOC (i.e. of solely microbial origin). It should be noted that the purpose of these evaluations has been to estimate the health risks in industrial work environments and processes where workers are exposed to much higher concentrations of one or a few of these chemicals. This contrasts with exposure to chemicals of microbial origin (e.g. in buildings with moisture and microbial damage) where people are exposed to a wide range of MVOCs, albeit at much lower concentrations.

The search requires further development of analytical methods. The other approach to increase the reliable interpretation of MVOC results might be to focus on statistical data handling of chromatograms.

Considering health effects of MVOCs, more *in vitro* and *in vivo* data on the inflammatory and other immunological responses to MVOCs are needed.

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Current Address: EVRIM OZKALE KAYA: Celal Bayar University, Faculty of Science and Letters, Biology Department, Manisa. Turkey.
E-mail : evrimmiko@gmail.com
ORCID: https://orcid.org/175012