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Review

The health significance of gas- and particle-phase terpene oxidation products: A review

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ABSTRACT

The reactions between terpenes and ozone (or other oxidants) produce a wide variety of both gas- and particle-phase products. Terpenes are biogenic volatile organic compounds (VOCs) that are also contained in many consumer products. Ozone is present indoors since it infiltrates into the indoor environment and is emitted by some office and consumer equipment. Some of the gaseous products formed are irritating to biological tissues, while the condensed-phase products have received attention due to their contribution to ambient fine particulate matter ($PM_{2.5}$) and its respective health significance. Despite common scientific questions, the indoor and ambient air research communities have tended to operate in isolation regarding this topic. This review critically evaluates the literature related to terpene oxidation products and attempts to synthesize results of indoor and ambient air studies to better understand the health significance of these materials and identify knowledge gaps. The review documents the results of a literature search covering terpene oxidation chemistry, epidemiological, toxicological, and controlled human exposure studies, as well as health studies focused more generically on secondary organic aerosol (SOA). The literature shows a clear role for gas-phase terpene oxidation products in adverse airway effects at high concentrations; however, whether these effects occur at more environmentally relevant levels is unclear. The evidence for toxicity of particle-phase products is less conclusive. Knowledge gaps and future research needs are outlined, and include the need for more consistency in study designs, incorporation of reaction product measurements into epidemiological studies conducted in both indoor and ambient settings, and more focused research on the toxicity of SOA, especially SOA of biogenic origin.

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Abbreviations: BAL, bronchoalveolar lavage; CCL-2, chemokine [C-C motif] ligand 2; CCL-5, chemokine [C-C motif] ligand 5; C/EBP, CCAAT/enhancer binding protein; CO-2, cyclooxygenase-2; CRP, C-reactive protein; EC, elemental carbon; EEP, end expiratory pause; EIP, end inspiratory pause; ET-1, endothelin-1; f, respiratory frequency; GM-CSF, granulocyte-macrophage colony stimulating factor; HO-1, heme oxygenase-1; IL-1α, interleukin-1-alpha; IL-1β, interleukin-1-beta; IL-6, interleukin-6; IL-8, interleukin-8; MAP kinase, mitogen activated protein kinase; MMP-9, matrix metalloproteinase 9; NF-κB, nuclear factor kappa beta; NOS-1, nitric oxide synthase-1; OC, organic carbon; PEF, peak expiratory flow; Penh, Enhanced Pause; PM, particulate matter; SOA, secondary organic aerosol; SOD, superoxide dismutase; sP-selectin, soluble platelet selectin; sTNF-RII, tumor necrosis factor receptor II; ST-segment depression, depression of the flatline segment running along the baseline of an EKG tracing; TB, time of brake; TGF-β1, transforming growth factor-beta 1; TI, inspiratory time; TIMP-2, tissue inhibitor of metalloproteinase-2; TE, expiratory time; TNF-α, tumor necrosis factor alpha; VOC, volatile organic compound; VT, tidal volume.

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1. Introduction

In recent years, there has been increasing interest in the potential health impacts of secondary organic compounds formed via terpene oxidation reactions. Such compounds include both gas-phase materials such as formaldehyde as well as particle-phase components such as pinic acid (Grosjean et al., 1992; Jang and Kamens, 1999). Interestingly, research related to this issue is divided based on the medium of interest, with both indoor air and ambient air researchers involved, often without knowledge of or interaction with the other. For example, at a recent indoor air meeting (Indoor Air 2011), there were a total of six papers on terpenes and/or secondary organic aerosol; however, these were all presented by researchers primarily involved in the indoor air field and were focused on indoor air sources, formation, and health effects. Conversely, at the American Association of Aerosol Research's 2012 annual meeting, there were 14 presentations on secondary organic aerosol (SOA) specifically related to terpenes, but none took an indoor air perspective. It would be helpful if the two research communities could share information in a more systematic way, as each discipline has much to learn from the other.

Indoor air research on terpene oxidation products was prompted in large part by the investigation of health complaints in indoor environments, including eye, nose, and throat irritation, dry skin, headaches, and other nonspecific symptoms (Wolkoff et al., 1997). Despite extensive epidemiological research on potential causes of these complaints, the cause of these symptoms remains elusive. Some hypotheses that have been considered include low levels of multiple volatile organic compounds (VOCs), low relative humidity, thermal comfort effects, and elevated CO_2 concentration indoors (Norback, 2009). More recently, the idea that reactions among indoor air pollutants can generate irritating compounds has been forwarded, and a number of studies have noted toxicological effects in animal models exposed to reaction products (e.g., Rohr et al., 2002; Sunil et al., 2007; Wolkoff et al., 1999, 2012).

There is also much interest in terpene oxidation from an ambient atmospheric chemistry perspective, particularly with respect to secondary organic aerosol. Secondary aerosol forms from gas-to-particle conversion processes, including nucleation, condensation, and heterogeneous and multiphase chemical reactions (Hallquist et al., 2009). Much attention has been focused on understanding the mechanisms of formation of SOA, identifying the products formed, modeling SOA formation at local and regional scales, and evaluating the impact of these aerosols on climate. Less attention has been given to investigating potential health effects from SOA exposure, although interest appears to be increasing in this area as understanding the role played by various particulate matter (PM) components in adverse health effects becomes a higher priority research topic. Currently, PM is regulated in the United States with a mass-based National Ambient Air Quality Standard (NAAQS), despite accumulating evidence that different components of PM have different inherent toxicity (e.g., Kelly and Fussel, 2012; Rohr and Wyzga, 2012). Knowledge of the health effects of other major PM components such as sulfate, nitrate, and elemental carbon is reasonably well-developed; however, the effects attributable to the organic carbon component, comprised of both primary aerosol and SOA, is less well understood (Mauderly and Chow, 2008).

This review attempts to bring together the two distinct sets of literature related to indoor and ambient air and critically evaluate, based on existing evidence, the potential for human health impacts from exposure to terpene oxidation products. It should be noted that the focus is on monoterpenes (and isoprene, a hemiterpene); little is known about the health impacts of sesquiterpenes or their oxidation products and thus they are not included in the scope.

2. Methods

An extensive search was conducted for published information related to terpene oxidation product epidemiological, toxicological, and

Table 1
Terpene concentrations measured in indoor air.

Reference	Location	α-Pinene (μg/m[a])	*d*-Limonene (μg/m[a])
Monteith et al. (1984)	Manufactured housing	12.5[b]	12.0[b]
Pellizzari et al. (1986)	Residential	1.4–3.4[c]	NM
Sheldon et al. (1988)	Office	2.6–19.4	NM
Girman et al. (1989)	Office	10–89	NM
Montgomery and Kalman (1989)	Residential	NM	6.6–35 (smkg); 1.6–77 (non-smkg)
Proctor (1989)	Office	1–11 (smkg); 2–8 (non-smkg)	1–31 (smkg); 0.4–8 (non-smkg)
Weschler et al. (1990)	Office	6.6–12.0	20.0–43.0
Proctor et al. (1991)	Personal exposure	0.6–116	0.3–72.0
Schleibinger et al. (2001)	Residential	23–44	33–65
Schlink et al. (2004)	Residential	13–2592	8–24,901
Sexton et al. (2004a, 2004b)	Residential	7[b]	16[b]
Tanaka-Kagawa et al. (2005)	Residential	<LOD[a]–650	<LOD–250
Vainiotalo et al. (2008)	Restaurant (smoking area)	NM	0.79–8.8
Vainiotalo et al. (2008)	Restaurant (non-smoking area)	NM	0.08–9.3
Jia et al. (2010)	Office	3.9[b]	5.5[b]
Jia et al. (2010)	Workplace[d]	4.2[b]	5.2[b]

Concentrations are expressed as ranges unless otherwise specified.
NM—not measured.
[a] LOD—limit of detection.
[b] Means reported in study.
[c] Range of medians for different regions.
[d] Workplaces included workshops, production centers, storage rooms, libraries, garages, and computer server rooms.