Respiratory effects of some key ozone-initiated terpene reaction products

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1 Introduction

There is an increasing concern about the use of consumer and household products, e.g. air fresheners and cleaning agents, in indoor environments, because of their content of terpenoid compounds (Anderson et al., 2010; Steinemann et al., 2011). Their ozone-initiated chemistry of in particular limonene (abundant and ubiquitous VOC indoors and a major ingredient in household/consumer products) readily undergoes gas-phase ozonolysis to produce a number of terpene oxidation products (OIRPs), gaseous, ultra fine particles, e.g. (Weschler and Shields, 1999). Surface ozonolysis of terpenoid compounds, e.g. sequi-terpenes in plants and skin oils (e.g. squalene), is also considered to be of health concern, e.g. in aircrafts (Wisthaler and Weschler, 2010). Respiratory effects of the upper airways are dominant, i.e. sensory irritation. Longer-lasting effects in the conducting airways have also been observed from OIRPs of limonene (Rohr et al., 2002; Wolkoff et al., 2008); the responsible OIRPs are unknown.

It has been hypothesized that some OIRPs have sensitizing properties (Anderson et al., 2007, 2010). Our objective was to investigate the respiratory effects of selected OIPRs.

2 Method/Materials

We have examined the upper/lower respiratory effects of some key OIRPs of common terpenoids. 4-acetyl-1-methylcyclohexene (4-AMCH) and isopropyl-6-oxo-heptanal (IPOH) are major OIRPs from limonene (Atkinson and Arey, 2003), and 6-methyl-5-heptene-2-one (6-MHO) and 4-oxopentanal (4-OPA) from e.g. geraniol and squalene (Forester and Wells, 2009).

4-AMCH and 6-MHO were from Aldrich and Aldrich-Sigma; purity > 95 %. IPOH and 4-OPA were synthesized according to (Wolinsky and Barker, 1960) and (Hutton et al., 2003), respectively; purity (> 95 %). Thorough GC/MS analyses were carried out to identify impurities. Chamber exposure concentrations were monitored by air sampling on Tenax TA followed by thermal desorption and GC/FID analysis. Five-point calibration of the compounds in methanol solutions was applied for determination of air concentrations ($R^2 \geq 0.99$), except for 4-OPA where pentane was used as solvent. Measured concentrations were within ± 15% of calculated concentration from 60 min dosage of the exposure chamber.

The respiratory effects of 30-60 min exposures were studied in a mouse bioassay, e.g. (Larsen et al., 2000). The bioassay allows detection of respiratory effects on the upper airways (i.e. sensory irritation), effects on the conducting airways and at the alveolar level (Alarie, 1998). RD_{50} values (the concentration that causes 50 % reduction of the respiratory rate) have been established and other parameters are obtained by computerizing the respiratory data, followed by analysis (Boylestein et al., 1995, 1996). Data are based on 3-5 different exposure levels around RD_{50}.

3 Results

The RD_{50} values can be used to predict LOAEL (lowest observed adverse effect level) and reference exposure levels (RELs) for sensory irritation in the general population (Kuwabara et al., 2007). Table 1 shows that LOAEL/REL values for 4-AMCH and 6-MHO are similar to that of limonene (Larsen et al., 2000), while IPOH was substantially more irritating.

Table 1. RD_{50}, LOAEL, REL values (mg/m^3).

Compound	RD_{50}	LOAEL	REL
(+)-Limonene	6000	392	54
4-AMCH	3390	240	24
6-MHO	6190	403	56
IPOH	~130	~15	~0.25
4-OPA	Not determined due to severe lung effects		

Severe and irreversible airflow limitation was observed for 4-OPA at ≤100 mg/m^3, thus RD_{50} was unobtainable. The effects in the conducting airways may be lung inflammation. 6-MHO also showed some unusual effect. Exposure experiments continue.

4 Conclusions

4-AMCH, 6-MHO and IPOH are reversible upper airway irritants like limonene, unlikely to cause lung effects in indoor environments. IPOH may in part explain the observed sensory irritation in the ozone-limonene system (Wolkoff et al., 2008). 4-OPA shows severe irreversible lung effects. It is possible that 4-OPA may explain effects in the conducting airways as reported by (Rohr et al., 2002; Wolkoff et al., 2008).

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