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SUMMARY

Thirdhand smoke (THS) is the residue from tobacco smoke that clings to virtually all surfaces long after a cigarette has been extinguished. The burning of tobacco releases many semi-volatile organic compounds (SVOCs) such as nicotine that adsorbs strongly onto indoor surfaces (walls, floors, carpeting, drapes, and furniture). Nicotine can persist on those materials for days, weeks, and even months. Our recent studies reveal that nicotine deposited on surfaces can react with other indoor pollutants, including ozone, which seeps in from outdoors, and nitrous acid, which is common in houses with gas-burning appliances. These reactions lead to the formation of carcinogenic tobacco-specific nitrosamines (TSNAs) and ultrafine particles (UFP < 100 nm) that could exacerbate or cause asthma. These findings shed light on the long-term exposure to residual tobacco smoke in indoor environments.

IMPLICATIONS

Our work highlights the importance of THS chemistry at indoor interfaces, particularly the production of nitrosamines and UFP with potential health impacts. Given the rapid sorption and persistence of high levels of nicotine on indoor surfaces –including clothing and human skin– these newly identified processes represent an unappreciated health hazard through dermal uptake, hand-to-mouth intake and inhalation of ultrafine particles.

KEYWORDS

Nicotine, Secondary Organic Aerosol (SOA), Tobacco Specific Nitrosamines, Asthma, Indoor Exposure

INTRODUCTION

Secondhand tobacco smoke (SHS, smoke inhaled unintentionally) is a major indoor source of human exposure to fine particles (Nazaroff 2004) and hazardous air pollutants (Nazaroff and Singer 2004; Charles et al. 2007), which are linked to adverse health effects such as chronic asthma, coronary heart disease, lung cancer, and chronic obstructive pulmonary disease (USDHHS 2006). It has been estimated that SHS causes as much as 2.7% of all deaths in the United States annually, and that its adverse health effects cost more than $25 billion annually in California alone (Repace 2007). Over the past decade, the US and other countries have successfully reduced the exposure of nonsmokers to SHS in public spaces and the workplace. Nevertheless, the US Surgeon General 2006 report warned that progress has been slower in the protection of young children, for whom the most important exposure setting is the home (USDHHS 2006).

While direct inhalation of SHS is an exposure pathway of concern, non-smokers, especially infants, are at risk through contact with surfaces and dust contaminated with residual smoke gases and particles (Matt et al. 2004; Matt et al. 2008). This type of lingering residue of tobacco smoke has recently been called thirdhand smoke (THS) (Winickoff et al. 2009). This paper reviews the emerging evidences on THS, its chemistry, its persistence in indoor environments and implications for pathways of exposure and health effects. We present findings from our recent studies on the reactions of atmospheric species (O_3, HONO, NOx) with residual smoke, particularly nicotine on surfaces (furniture, walls, skin, clothing) as a source of long term exposure to harmful pollutants (Destaillats et al. 2006; Petrick et al. 2010; Sleiman et al. 2010; Sleiman et al. 2010).

METHODS

a. Study design and experimental for nicotine reactions with HONO

Laboratory experiments were carried out using cellulose paper (Whatman Cat. No. 3030-153) as indoor model surface to test the formation of TSNAs from HONO reactions with sorbed nicotine and SHS. Cellulose substrates were exposed to vaporized nicotine in a tubular flow reactor, obtaining a loading of 9.1 µg cm^{-2}, before equilibration with HONO (65 ppbv). SHS coated cellulose substrates were collected in an LBNL room-sized 18-m^3 environmental chamber with low background concentrations of airborne contaminants. SHS was generated in the chamber using a smoking machine (ADL/II smoking system, Arthur D. Little, Inc.). Nine cigarettes of a major US brand were smoked at equal intervals over a 3-h period. The main experimental conditions for the chamber test are described elsewhere (Sleiman, Gundel et al. 2010). In addition, two samples were collected inside the passenger compartment of a light duty pick-up truck in which the driver routinely smoked while commuting. The cellulose was exposed to SHS over the next 3 days during which the driver smoked 34 cigarettes inside the vehicle. Extracts were analyzed by gas chromatography – ion trap – tandem mass spectrometry (GC-IT-MS/MS) using a Varian 3800 gas chromatograph (Varian Chromatography Systems, Walnut Creek, CA, USA). Additional experimental details are reported in (Sleiman et al. 2009). All analyses were replicated. Uncertainties and limits of detection were derived from replicates and blanks using accepted statistical methods. Experimental errors were in the range 5-30 %.

b. Study design and experimental for ozone reactions with Nicotine and SHS

SHS was generated in an 18-m^3 environmental chamber by smoldering 10 cigarettes from a leading US brand. During the first 15 minutes after smoking started the diluted smoke was pumped into evacuated 100-L tedlar bags to about 40% capacity. In separate experiments, 5 µL (30 µmoles) of liquid nicotine (Sigma Aldrich, purity 99%) was injected into two 20-L tedlar bags, one with 10-L dry air (RH ~ 0 %) and the other with 10-L humidified air (RH ~ 50 %). Ozone was generated by UV irradiation (UVP Inc.) of pure air, diluted with dry or humidified air to reach concentrations in the range of (50 - 150 ppbv) and introduced into the tedlar bags previously filled either with SHS or pure nicotine. Tedlar bags containing fresh or ozonated SHS and nicotine were connected without further dilution to a scanning mobility particle sizer (SMPS, model 3936, TSI, Shoreview, MN) and to a vacuum ultravioled aerosol mass spectrometer (Gloaguen et al. 2006) available at the Advanced Light Source (ALS) at Lawrence Berkeley National Laboratory.

RESULTS

Formation of Tobacco specific nitrosamines in HONO-nicotine reactions

Three main TSNAs are formed in the reaction of sorbed nicotine and gaseous HONO: 1-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridinyl)-4-butanal) **(NNA),** 4-(methylnitrosamino)-1-(3-pyridil)-1-butanone **(NNK)** and *N*-nitroso nornicotine **(NNN)**. In field measurements, we detected TSNAs on interior surfaces of a truck driven by a heavy smoker. Fig. 1A shows the concentrations of surface-bound TSNAs on the stainless-steel glove compartment (**Truck-A**), and on cellulose substrates attached next to it (**Truck-B**), for 3 days in which smoking occurred in the vehicle. In both samples, two TSNAs, NNA and NNK, were detected at appreciable levels (1 to 5 ng cm^{-2}). Proposed mechanism for the formation of TSNA is shown in our recent PNAS paper (Sleiman, Gundel et al. 2010).

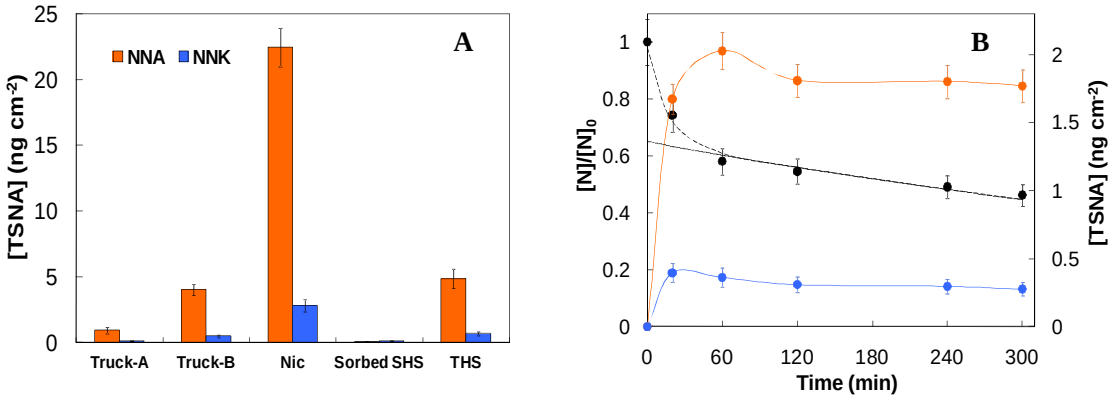

Figure 1. Surface concentrations of NNA and NNK in laboratory and field experiments (A) and time course of nicotine loss and production of NNA and NNK in presence of HONO (B).

Similar results were found when cellulose substrates containing nicotine (sample **Nic**, Fig. 1A) and sorbed tobacco smoke (**Sorbed SHS**) were exposed to HONO for 3 hours. In the resulting sample (**THS**), TSNA surface concentrations increased at least 10-fold. Furthermore, in all samples exposed to HONO (**THS**, **Nic**, **Truck-A**, **Truck-B),** the steady-state ratio of total TSNA concentrations to surface nicotine expressed in mass units was about 1:250 (equivalent to 1:320 in mole units), corresponding to nicotine conversions of χ_{NNA} = [NNA] / [N] = 3.5×10^{-3} and χ_{NNK} = [NNK] / [N] = 0.5×10^{-3} (for concentrations expressed in mass units). Fig. 1B shows time-concentration profiles for surface nicotine and TSNAs in laboratory experiments. Both NNA and NNK formed rapidly, reaching maximum concentrations within the first hour. Formation rates of TSNAs were $R_{NNA} = \partial[NNA]/\partial t$ = (8.4 ± 0.6)10^{-2} ng cm^{-2} min^{-1} (0.24 ± 0.02 μmol m^{-2} h^{-1}) and $R_{NNK} = \partial[NNK]/\partial t$ = (2.0 ± 0.4) 10^{-2} ng cm^{-2} min^{-1} (0.06 ± 0.01 μmol m^{-2} h^{-1}), respectively, estimated from the initial slope (t < 20 min) in Fig 1B, assuming that the initial decomposition rate was negligible. A bi-exponential model was fitted to the surface nicotine concentration profile to estimate contributions from chemical reaction and desorption. The fitted rate constant for nicotine reaction of k_N = 1.25×10^{-3} min^{-1} corresponds to nicotine reactive loss rates in the range $R_N = -\partial[N]_S/\partial t$ = 1.5 – 1.1 ng cm^{-2} min^{-1} (5.5 – 4.1 μmol m^{-2} h^{-1}). The nicotine reaction rate was almost identical to the HONO reactive uptake rate (R_{HONO} = 5.5 μmol m^{-2} h^{-1}) corresponding to a HONO deposition velocity of 2.1 m h^{-1}. This value is the same order of magnitude as the boundary-

layer mass transfer coefficient in buildings (Morrison et al. 2006), suggesting that reaction with nicotine may be a strong sink for HONO indoors. Assuming first-order reaction kinetics, the relative yield (ϕ_{TSNA}) for the sum ofTSNAs can be estimated from initial reaction rates as:

$$\phi_{TSNA} = \frac{R_{NNA} + R_{NNK}}{R_N} * 100 \qquad (1)$$

Total TSNA yields were ϕ_{TSNA} = 6.7 to 9.1% by mass (5.4 to 7.3% by mole). These relatively high yields call attention to the importance of this reaction as a source of tobacco carcinogens on indoor surfaces.

Formation of secondary organic aerosols in ozone-nicotine reactions

Bags filled with nicotine alone showed no formation of particles via nucleation or condensation processes, whereas exposure to ozone led to formation of significant amounts of SOA, as illustrated in

Figure 2.

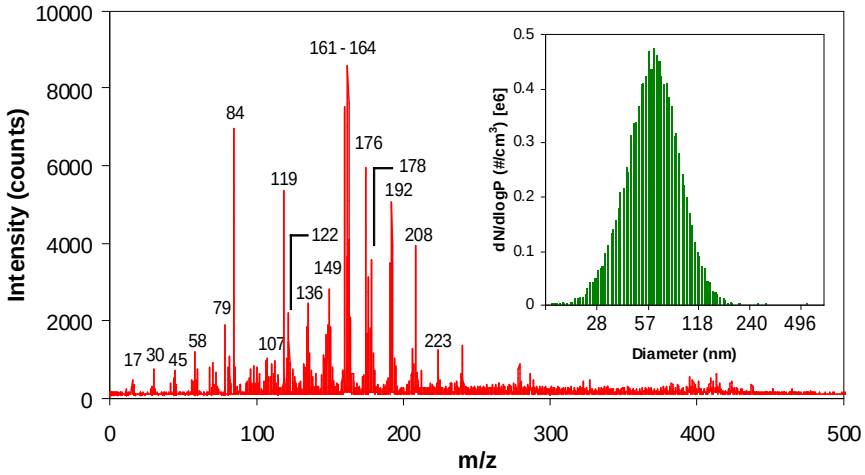

Figure 2. VUV mass spectra (VUV energy: 10.4 eV) and SMPS size distribution of secondary organic aerosol generated during nicotine reaction with ozone.

This finding suggests that gas phase nicotine, in the presence of ozone, could contribute

significantly to the production of SOA during the aging of tobacco smoke. SOA was formed in both dry and humid air conditions. However, in presence of water vapor, SOA formation was enhanced and median particle size was increased from 76 nm to 200 nm. This may be related to an increase in water soluble organic carbon (WSOC) that partitions to the particle phase. Assuming that the formation of SOA was mainly due to gas phase reactions between nicotine and ozone, we obtained aerosol yield Y = 3.8% and Y = 9.2% under dry and humid conditions, respectively. Surface reaction between sorbed nicotine and ozone could be also a significant source of SOA (Petrick et al. 2011). Proposed molecular structures for the main peaks observed in Figure 2 and their formation mechanisms are described in our recent paper (Sleiman, Destaillats et al. 2010). In addition, we also found that chemicals in SHS react with O_3 to produce particles that could exacerbate asthma. Exposure of SHS to ozone induced the formation of ultrafine particles (< 100 nm) at 8-times higher levels than in freshly emitted smoke. These particles contained high molecular weight nitrogenated species (m/z 400-500) that could be formed by accretion/acid-base reactions as described in (Sleiman, Destaillats et al. 2010).

DISCUSSION - IMPLICATIONS FOR INDOOR EXPOSURES

The *in situ* formation of TSNAs presents a specific concern about the hazards of thirdhand smoke. NNK is a strong carcinogen, with reported cancer potency of 49 kg mg^{-1} d^{-1} (Pankow et al. 2007). NNA carcinogenicity has not been reported, but its mutagenic activity is similar to that of NNN. There are several potentially important exposure routes through which surface-formed TSNAs may enter the body. Direct inhalation of gas-phase TSNAs is likely negligible, given their very low vapor pressures (in pressure units of mm Hg, $Log_{10}P°_{NNA}$ = -6.67 and $Log_{10}P°_{NNK}$ = -6.72. Instead, dermal contact with surfaces contaminated by TSNAs (skin, clothing and furnishings), as well as inhalation and ingestion of TSNA-loaded dust, are likely the main exposure pathways. Nicotine surface concentrations ranging from 5 to 100 μg m^{-2} have been measured in dust, on surfaces inside vehicles (dashboards) (Matt, Quintana et al. 2008), and in households of smokers (tables and bed frames) (Matt, Quintana et al. 2004). In the presence of HONO, surface-bound nicotine could react to produce TSNAs at surface concentrations in the range of 5- 4000 $ng.m^{-2}$. More details about the estimations of TSNA levels are shown in our recent paper (Sleiman, Gundel et al. 2010). Given the low volatility of TSNAs and the high levels of nicotine typically found in environments contaminated with tobacco smoke, these carcinogens can persist indoors and on the human envelope. Due to their frequent contact with surfaces and dust, infants and children are particularly at risk. At approximately 0.05–0.25 g day^{-1}, the dust ingestion rate in infants is estimated to be more than twice that of adults (Matt, Quintana et al. 2004). Moreover, considering that infants have a higher respiration rates (by a factor of 3–8) and a lower body weights than adults (by a factor of 10–20), even low doses of TSNAs may represent a potential long term health hazard.

Additionally, based on the hazard prediction model developed by (Jarvis et al. 2005), most of SOA constituents were found to exhibit high asthma hazard index (AHI) in the range 0.7 – 1 (0: no hazard; 1: maximum hazard), indicating that these SOA are likely to cause or exacerbate asthma (Sleiman, Destaillats et al. 2010). As consequence, interaction between indoor pollutants such as SHS or residual nicotine and O_3 needs to be taken into account for better THS exposure assessment. Our findings support recommendations from the California EPA and the Air Resources Board that discourage the use of ozone-generating “air purifiers,” which among other applications, have been used for the removal of tobacco odors.

CONCLUSIONS

The chemistry described here could increase the hazards associated with exposure to THS by increasing the likelihood of respiratory effects and cancer risk that are linked to formation of UFP, and carcinogenic TSNAs, respectively. Implementation of 100% smoke-free environments in public places and self-restrictions in residences and automobiles are the most effective tobacco control measures, through elimination of the primary pollution source. In buildings where substantial smoking has occurred, replacing nicotine-laden furnishings, carpets and wallboard can significantly reduce exposures to THS hazards. More research is needed on the identification and characterization of specific biomarkers to assess human intake of THS and to better understand their health implications.

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