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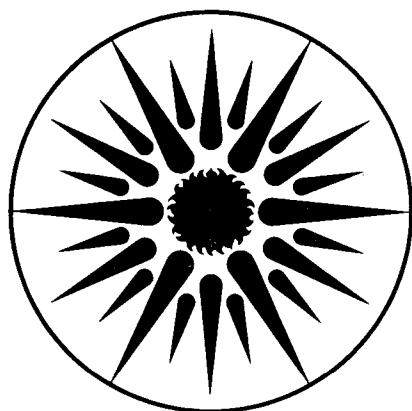
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**Volatile N-nitrosamines in Environmental Tobacco Smoke:
Sampling, Analysis, Emission Factors and Indoor Air Exposures**

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Abstract

A more convenient sampling and analysis method for the volatile N-nitrosamines (VNA) in ETS, using commercially available ThermoSorb/N cartridges, was developed and validated. Using the method, emission factors for the two major VNA in environmental tobacco smoke (ETS) were determined in a room-sized environmental chamber for six commercial cigarette brands, which together accounted for 62.5% of the total market in California in 1990. The average emission factors were 565 ± 115 and 104 ± 20 ng per cigarette for N-nitrosodimethylamine and N-nitrosopyrrolidine, respectively.

The emission factors were used to estimate VNA exposures from ETS in a typical office building and an average residence. Indoor concentrations of N,N-dimethylnitrosamine from ETS for these scenarios were less than 10% of the reported median outdoor concentration. This median outdoor concentration, however, includes many measurements made in source-dominated areas and may be considerably higher than one based on more representative sampling of outdoor air.

Key Words: N-nitrosamines, environmental tobacco smoke; emission factors, indoor air, cigarettes, N,N-dimethylnitrosamine

Introduction

Exposures to environmental tobacco smoke (ETS) are widespread in the population. A recent study conducted in California indicates that approximately 62% of adults and adolescents in that state are exposed to ETS for an average of 5 hours per day (1,2). The volatile N-nitrosamines (VNA) in ETS are one of the classes of toxic air contaminants that are of particular concern because of their carcinogenicity. Among the VNA present in tobacco smoke, N-nitrosodimethylamine (NDMA) and N-nitrosopyrrolidine (NPYR) occur in the highest concentrations (3). N-nitrosodiethylamine (NDEA) and N-nitrosoethylmethylamine (NEMA) have also been reported in tobacco smoke (4), although at much lower concentrations. NDMA, NEMA, and NDEA are among the most potent environmental carcinogens in this group of compounds. NDMA and N-nitrosomorpholine (NMOR) are listed as

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hazardous air pollutants in the Clean Air Act Amendments of 1990 and have been designated as toxic air contaminants by the California Air Resources Board.

Although there is evidence of widespread indoor exposures to VNA from ETS (5-10), most reported data are not sufficiently complete to infer the distribution of exposures for the general population. For example, available indoor concentration measurements are limited to a few high exposure situations and, because other measurements, such as air exchange rates, were not made simultaneously, emission factors cannot be inferred for extrapolation to other indoor settings or smoking rates (7-10).

Emission factors that have been determined are for sidestream smoke (SS) (3-6, 11-12), the smoke freshly emitted by the smoldering end of a cigarette between puffs, rather than ETS, the smoke to which non-smokers are exposed when they are in an indoor environment with smokers. ETS is composed largely of sidestream tobacco smoke, with minor contributions from exhaled mainstream smoke (the smoke from the cigarette which is directly inhaled by the smoker) and any smoke that escapes from the burning part of the tobacco during puff-drawing by the smoker. ETS differs from SS in that it is highly diluted and dispersed within a room and it undergoes aging. Thus, emission factors for ETS may differ from those measured for SS. In addition, because of changes in recent years in the cigarette manufacturing process to reduce tar in mainstream smoke, e.g., use of more reconstituted tobacco, the SS emission factors for VNA reported in the older literature may differ from those for cigarettes currently in the market.

The objectives of this research were to determine the average, range and variability of VNA emission factors (ng per cigarette) for ETS among a subset of popular cigarette brands which have large market shares in California and to use these factors to estimate exposures for selected typical indoor scenarios. In the course of this work, a more convenient sampling and analysis method for the VNA in ETS was developed and validated.

Experimental Methods

Six commercial cigarette brands representing a combined market share of 62.5% of the cigarettes sold in California in 1990 (13) and a University of Kentucky reference cigarette (1R4F) were used for the study. The commercial cigarettes included five filtered brands and one unfiltered brand; two of the brands were mentholated and one was low-tar. Prior to smoking, all cigarettes were conditioned for at least 48 hours at 60% relative humidity and room temperature over a solution of saturated sodium bromide in a dessicator. The average mass of the tobacco per cm of length for each brand was determined by cutting off the butt section of six equilibrated cigarettes and weighing the tobacco in the remaining portion (14).

For the chamber experiments, three cigarettes were smoked in sequence in the chamber, each for 8 to 9 minutes, using a single-port smoking machine (ADL/II smoking system, Arthur D. Little, Inc.) attached to a sequential twelve-port cigarette holder. The custom-designed and fabricated holder was programmable and had auto-igniting and extinguishing capabilities. A standard smoking cycle of one puff per minute of 35-cm³ volume and 2-second duration was used. The sidestream smoke was emitted into the chamber to simulate ETS. The mainstream smoke was vented outside of the chamber. The filter

cigarettes were smoked to a butt length equal to filter overwrap plus 3 mm, while the non-filtered cigarettes were smoked to a 23-mm butt length. The mass of the cigarette tobacco smoked in each experiment was calculated from the average mass of tobacco per unit length and the actual smoked length of the cigarette.

The 20-m³ environmental chamber used for these experiments was designed specifically to provide a controlled environment with low background concentrations of airborne contaminants. It is constructed of low-emitting materials and its interior is clad with stainless steel. Inlet air, drawn from outside the building by a variable-speed blower, is passed through a coarse filter, a charcoal filter, and a HEPA filter, in series. The chamber was operated in the static mode (i.e., no mechanical ventilation) with an air exchange rate of 0.005 h⁻¹ due to infiltration and 0.024 h⁻¹ due to removal of air for sampling. The chamber temperature and relative humidity averaged 23.7 ± 0.8 °C and 45.7 ± 3.1 %, respectively, for the nine chamber experiments.

The smoking machine and holder were placed in one corner of the chamber, about two feet from each vertical wall. The chamber air was mixed throughout the experiment by six small axial fans, mounted on the chamber walls alternately at 1/3 and 2/3 of the height of the wall. Air samples were drawn from the center of the chamber for sampling. Sampling for VNA started immediately after the third cigarette was extinguished and continued for a period of 250 minutes. The sampler consisted of an open-face Teflon filter (Gelman Sciences) for particles followed by a Thermosorb/N cartridge (Thermedics Detection, Inc.). The flow rate of 4 L min⁻¹ was regulated with an electronic mass flow controller and vacuum pump.

Standard compounds, solvents, and cartridges were used as purchased from the manufacturers. The N-nitrosamine standard compounds were purchased from the following suppliers: NDEA (98%) from Pfaltz & Bauer, NMOR (98%) from Sigma Chemical Co., and NPYR (99%) and NDMA (99%) from Aldrich Chemical Co. Standard solutions of the N-nitrosamines were prepared in dichloromethane (DCM) at µg ml⁻¹ levels and working solutions were prepared by appropriate dilution. Both the standards and liquid samples were kept in the dark and refrigerated. Standards and samples were brought to room temperature and sonicated for 5 minutes before use.

Four VNA were initially targeted for measurements in ETS: NDMA, NDEA, NPYR and NMOR. In some initial experiments, we found that NDEA was present at concentrations that were at least 10-times lower than the concentration of NDMA and below the limits of detection for the optimal sample size required for measuring the other VNAs in the chamber. Because of constraints in the number of samples that could be collected and analyzed, emission factors were determined only for NDMA and NPYR, the VNA present at the highest concentrations. NDEA was used as the internal standard for analysis because it was not detectable in the ETS samples and it eluted between NDMA and NPYR with good resolution and peak shape. There was no evidence for the presence of NMOR, even with larger samples. NMOR was used in the standard mixture during the preliminary experiments.

After collection, the sample-loaded Thermosorb/N cartridge was spiked with the 73 ng of NDEA, the internal standard. The cartridge was coupled at the outlet to an alumina-B Sep-pak (Waters Chromatography, Inc.) and 1.5 ml of 33% methanol in chloroform was added to the cartridge. The sample and nitrosating inhibiting agent in the cartridge were allowed to dissolve in the solvent for a minute. A 5 ml aliquot of 10% chloroform in DCM was then added to the cartridge and air pressure was

used to elute the solution from the cartridge to the coupled Sep-pak. The cartridge and Sep-pak were separated and the cleaned extract was recovered from the Sep-pak using more air pressure. The extract was concentrated in a rotary evaporator to 0.5 ml and analyzed. No detectable background VNA were found in blank Thermosorb/N cartridges, alumina Sep-paks or in the organic solvents (Baxter Healthcare Corporation).

A Hewlett-Packard 5890A gas chromatograph (GC) equipped with a capillary DB-Wax column (length 30 m, ID 0.32 mm, film thickness 0.25 micron; J&W Scientific, Inc.) was used for the analysis. A thermal energy analyzer (TEA Model 543; Thermedetec Inc.), was used for detection. Helium was used as the carrier gas (column head pressure 103 kPa) and 2- μ l samples were injected for the analysis. The temperature program started at 50 °C and was held for 2 minute, then ramped at 8 °C min⁻¹ for 15 minutes to 180 °C and then held for another 3 minute. Under these separation conditions, the retention times of NDMA, NDEA, NPYR and NMOR were 4.2, 5.3, 10.8 and 11.7 minutes, respectively. The GC-TEA interface was maintained at 225 °C, and the furnace of the TEA was operated at 550 °C. Oxygen flow to the TEA was regulated at 30 ml min⁻¹ and ozone flow to the vacuum chamber was adjusted to 0.2 kPa at 50 °C.

Method Development and Validation

Considerations

Airborne N-nitrosamines are difficult to measure reliably due to the potential for creation or loss of N-nitrosamines during sample collection. Nitrogen dioxide and free amines in an air sample can react to create new N-nitrosamines as artifacts. Losses can occur due to the degradation of N-nitrosamines from exposure to ultraviolet light and to the breakthrough of the compounds from the sampling media.

The most highly developed and validated method for sampling VNA from tobacco smoke employs an aqueous buffered solution (pH = 4.5 citrate-phosphate) with 20 mM ascorbic acid contained in several serially-connected impingers (4-7, 11, 12, 15). Ascorbic acid is added to the solution as a nitrosating inhibitor to prevent the formation of artifact N-nitrosamines from the amines and NO_x in tobacco smoke (16). This method is limited in air flow rate (especially for midjet-impingers) and an aqueous solution is not a very convenient sampling medium, particularly for field experiments. Sample recovery problems are often encountered in liquid-liquid extraction from the aqueous buffers as well as problems such as the emulsion formation. Labor intensive sample preparation procedures and the relatively fast degradation of the aqueous ascorbic acid solution are two additional drawbacks to the use of this sampling method. Among the other N-nitrosamine collection methods, use of wet traps such as 1N KOH, cold traps and Tenax traps have been reported, each with its' own limitations (17, 18).

Thermosorb/N cartridges are commercially available sampling cartridges which have been specifically designed for the quantitative collection of N-nitrosamines in outdoor air (19, 20). These cartridges eliminate the most common problems associated with the aqueous sampling medium. Prior to this study, the cartridges had not been evaluated for N-nitrosamines in such a complex matrix as environmental tobacco smoke. The cartridge contains two sorbent zones, the first of which selectively traps and removes amines from the incoming air and prevents the subsequent nitrosamine formation by airborne nitrogen oxides, while the second zone contains a chemical nitrosating inhibitor system which prevents N-nitrosamine formation following elution of the Thermosorb/N cartridge (21). The cartridges

have a relatively moderate sampling capacity (1500 ng per cartridge); however, they can be connected in series to increase the total capacity of the sampling system.

Recovery of VNA from Sampling Media

The efficiency of VNA recovery from Thermosorb/N cartridges was evaluated by spiking aliquots of the standard mixture onto the cartridges and then drying the cartridges by passing dry air through them. The dried cartridges were each eluted with 2 ml of 33% methanol (v:v) in DCM.

For comparison, VNA recoveries from the impinger solutions were also determined. Fifteen ml of the aqueous trapping solution was spiked with an aliquot of the standard VNA solution. The spiked solution was then extracted with 2 x 3 ml of 10% chloroform in DCM. The organic layer was separated from the aqueous solution and passed first through a column containing 5 g of anhydrous sodium sulfate to eliminate water and then through a coupled alumina-B column for clean-up. Once all of the organic solvent passed through the coupled columns, a 2-ml aliquot of 33% methanol in DCM was used to elute the remaining VNA sorbed on the alumina-B Sep-pak column. Air pressure was applied to recover the VNA.

The results of these experiments are presented in Table 1. Recoveries were high (generally > 90%) from both the Thermosorb/N cartridges and the impingers. Recovery of NDMA from the impinger solution was slightly lower than for the other VNA.

Sample Breakthrough

Breakthrough of VNA from the Thermosorb/N cartridges was evaluated by pulling room air through a VNA-spiked Thermosorb/N cartridge for 250 min at a flow rate of 4 L min⁻¹. The flow rate, air sample volume and the mass of VNA spiked approximated the mass expected for sampling of VNA in ETS in the chamber. Another Thermosorb/N cartridge was connected in series downstream of the spiked cartridge to collect any breakthrough. No detectable levels of VNA were found in the downstream collection cartridge when the spiked cartridge was thoroughly dried. However, breakthrough of VNA was observed if any solvent from the spiking was left in the cartridge. Breakthrough was further evaluated by sampling VNA in ETS in the chamber using two Thermosorb/N cartridges in series. No VNA was detected in the downstream cartridge. It was concluded that use of a single Thermosorb/N cartridge was justified for sampling under the conditions of our experiments.

Artifact Formation

In situ artifact formation of N-nitrosamines in the Thermosorb/N cartridges has been tested by Rounbehler *et al.* (21) by passing an air stream containing oxides of nitrogen (NO_x) through a cartridge spiked with the amine precursors of the N-nitrosamines. This simulated an artifact formation situation for outdoor air. They did not detect any N-nitrosamines, and thus, concluded that the cartridges are artifact free (21). We did not repeat this experiment. However, we did evaluate Thermosorb/N cartridges for artifact formation when used for sampling VNA in tobacco smoke. This was done by comparing the cartridge method with the aqueous solution-impinger method that has been validated for sampling tobacco smoke. For sampling, a Thermosorb/N cartridge was placed behind an open-faced Cambridge filter to remove particles. The reference sampling line consisted of three midjet-impingers in series, each having 15 ml of pH 4.5 citrate-phosphate buffer with 20 mM ascorbic acid, placed downstream of an open-face Cambridge filter. The Cambridge filters were impregnated with ascorbic acid to avoid any artifact formation as the samples passed through the filter. ETS samples were collected

from the environmental chamber (the air exchange rate was 0.22 h^{-1} in this experiment) at 2 L min^{-1} for 250 minutes for trials No. 1 and 3 and for 300 minutes for trial No. 2. The results of the three trials comparing the two methods are presented in Table 2.

For NPYR, the average emission factors determined by the two methods did not differ significantly ($p < 0.05$). There was, however, a statistically significant difference in the average emission factors of NDMA. The difference is probably not due to artifact formation in the cartridge but rather due to a slightly lower recovery of NDMA from the impinger solution, as shown in the recovery studies in Table 1. Consequently, we concluded that the Thermosorb/N cartridge would be suitable for sampling VNA in ETS and would provide emission factors comparable to those obtained by the impinger method.

Besides the Thermosorb/N cartridges and impinger solutions, the impregnated Cambridge filters used for sampling were also analyzed for VNA. The filters were spiked with internal standard, cut into eight pieces, immersed in 10 ml of 10% chloroform in DCM, and sonicated for 30 minutes. The extract was passed through an alumina-B Sep-pak column and the cleaned extract was concentrated to a final volume of 0.5 ml. An aliquot of the extract was analyzed. No detectable levels of NDMA and NPYR were recovered from the filters. Recovery of the internal standard was $92 \pm 7\%$ (S.D.). Therefore, it was concluded that the filter did not remove the VNA from the ETS sample. The impregnated Cambridge filter was replaced by a Teflon filter in subsequent sampling. A Teflon filter provides better estimates of the particulate mass in ETS than the Cambridge filter which has a tendency to adsorb the water vapor in the emissions resulting in higher uncertainty in the particulate mass. Several particulate-loaded Teflon filters were also extracted and analyzed, but no VNA were found.

Development of a Sample Clean-up Method for VNA Collected on Thermosorb/N Cartridges

For sample recovery, the Thermosorb/N cartridges were back flushed with 2 ml of 33% methanol in DCM, following the manufacturer's recommendation that VNA loaded cartridges be back flushed with a polar solvent such as methanol, acetone or a mixture of DCM or chloroform with methanol or acetone. The manufacturer also suggested that the extracts could be analyzed without a sample clean-up procedure (22). This may be acceptable for VNA samples from less complex sample matrices. However, for ETS samples, the extracts contaminated the capillary GC column and interfered in later analyses. We suspected that the problem was due to the elution of polar ETS compounds from the cartridge. Several different strategies were tried to minimize these interferences.

We first attempted to develop a more selective procedure to minimize the extraction of polar interferences by using different solvents. Neither DCM nor chloroform could completely extract VNA from the cartridge. Other non-polar solvents, such as n-hexane, were also not efficient for the extraction. Acetonitrile was a moderately efficient solvent for extraction but required a significantly larger solvent volume. Other polar solvents, such as acetone, completely recovered the VNA but also extracted polar compounds.

Efforts were then made to eliminate polar interferences in the extracts using a sample clean-up procedure. The extract in methanol was concentrated to about 0.5 mL on a rotary evaporator, loaded onto an alumina-B Sep-pak, and allowed to dry in air for 5-6 hours to eliminate methanol, taking care not to expose the extract to light. We did not attempt to dry the solvent by purging the Sep-pak with a gas since we found breakthroughs of VNA when air is passed through a cartridge containing residual solvent. The air-dried Sep-pak was eluted with 5 ml of 10% chloroform in DCM to recover VNA, leaving the

polar interfering compounds on the Sep-pak. The eluate was then reduced to 0.5 ml using a rotary evaporator. Although this procedure yielded a cleaner extract, significant losses of some VNA were observed, possibly due to volatilization during the two concentration steps. A modified extraction-clean-up procedure was finally developed which solved the polar interference and the loss problems.

In the modified extraction-clean-up procedure, the sample-loaded Thermosorb/N cartridge was spiked with 73 ng of NDEA, the internal standard. Then the cartridge was coupled to an alumina-B Sep-pak and 1.5 ml of 33% methanol in chloroform was added to the cartridge. The sample and nitrosating inhibiting agent were allowed to dissolve in the solvent for one minute. A 5-ml aliquot of 10% chloroform in DCM was then added to the cartridge and air pressure was used to elute the solution from the cartridge to the coupled Sep-pak. The cartridge was separated from the Sep-pak and the cleaned extract was recovered from the Sep-pak using more air pressure. The extract was concentrated in a rotary evaporator to 0.5 ml and analyzed. Extracts prepared by this procedure were cleaner as no chromatographic problems were observed during VNA analysis. The procedure yielded a $97.8 \pm 2.8\%$ (S.D.) recovery of the internal standard, NDEA, from nine cartridges loaded with ETS samples.

Limit of Detection and Overall Sensitivity of the Method

The sensitivities of the analytical detection method, estimated as three times the background noise, were 10, 14 and 14 pg per injection for NDMA, NDEA and NPYR respectively. The sampling volumes were 1 m³ per sample, and the chamber volume was 20 m³. The extract were concentrated to a final volume of 0.5 ml and 2- μ l aliquots were analyzed. Therefore, the estimated limits of detection were 17, 23 and 23 ng per cigarette for NDMA, NDEA and NPYR, respectively.

Emission Factors for VNA in Environmental Tobacco Smoke

A time dependent mass-balance model (23) was used to calculate the emission factors, E (ng per cigarette), from the measured average airborne VNA concentrations, C_m (ng m⁻³). The model was based on the following basic assumptions. First, the only VNA source in the chamber is cigarette smoking. Analysis of background chamber samples confirmed this assumption. Second, VNA concentrations in the chamber follow a first-order exponential decay with time due to air infiltration and sampling, i.e., there are no VNA losses due to degradation or deposition to the chamber surfaces. Finally, the model assumes complete mixing of the air in the chamber. This was ensured by the use of mixing fans mounted on the walls. The relationship between E and C_m is,

$$E = [C_m V a \Delta t] / [N (e^{-at_i} - e^{-at_f})] \quad (1)$$

where V is the volume of the chamber (m³), a is the air infiltration rate (h⁻¹); $\Delta t = t_f - t_i$ where t_f and t_i (h) are the final and initial sampling times; and N is the number of cigarettes smoked. The infiltration rate for the chamber operated in static mode was determined prior to the ETS experiments by spiking sulfur hexafluoride (SF₆) into the chamber and following its' rate of decay. This was 0.005 h⁻¹. During the ETS experiments, there was additional infiltration due to the removal of air by sampling. Therefore, the total air infiltration rate, a, was the sum of the two removal mechanisms.

Table 3 summarizes the emission factors determined for NDMA and NPYR in ETS from the six commercial brands of cigarettes and from the 1R4F reference cigarette. The standard smoked length and

the mass of tobacco per unit length for each of the cigarette brands are also reported in Table 3. The average emission factors for NDMA and NPYR for the six commercial cigarettes were 565 ± 115 (S.D.) and 104 ± 20 (S.D.) ng per cigarette, respectively. Duplicate chamber experiments were conducted for brand A and the reference cigarette, as shown in Table 3. The variabilities in the duplicate chamber measurements for both NDMA and NPYR were within the uncertainties estimated for the sampling and analysis method (about 13% for each VNA) using the propagation of errors method (23). This indicates that the small variations in the chamber operating conditions introduced very little additional uncertainty.

The coefficient of variation for the average ETS emission factors for the six commercial brands was only 20% for both NDMA and NPYR. This variability is relatively small compared to the variability in mainstream smoke emission factors for these compounds which has been reported to be as large as two orders of magnitude across brands (5). The highest ETS emission factors for NDMA and NPYR were 1.7 times higher than the lowest values. Within that small range, cigarettes E and F had the highest ETS emission factors for both the compounds, as might be expected since these were the longest cigarettes. The ETS emission factors for the reference cigarette 1R4F, which is manufactured to reflect current U.S. market shares of various cigarettes (except extra-light types), fell within the ranges for the six commercial brands. If the ETS emission factors are compared in terms of ng of VNA emitted per mg of tobacco consumed, the variability among the brands is even smaller, with coefficients of variation of only 12 and 10% for NDMA and NPYR, respectively. The ratio of the highest to the lowest emission factor for the six brands was only about 1.4 on this basis.

Cigarette B was the only "light" cigarette tested and it yielded the highest ng of VNA per mg of tobacco consumed as well as a higher ng per cigarette value than its "regular" counterpart, cigarette A. In developing the sampling and analysis method for VNA, we used the light counterpart of cigarette D which was not used in main study. The ETS emission factors for this light brand (581 and 142 ng per cigarette for NDMA and NPYR, respectively) were also higher than for cigarette D, (447 and 100 ng per cigarette for NDMA and NPYR, respectively). These differences between regular and light cigarettes are significant within the estimated variability due to sampling and analysis. Such a difference is plausible because higher proportions of stems and ribs of the tobacco leaf are used in light cigarettes. These parts of tobacco leaf are rich in nitrate which has been shown to be an important determinant of VNA yields (4, 24-25).

A direct comparison of the VNA emission factors measured in this study with values previously reported in the literature is not possible for several reasons. First of all, the cigarette manufacturing process has changed during the last decade. Nowadays more reconstituted tobacco is used to reduce the tar levels in mainstream smoke. In addition, criteria for brand selection, smoking protocols, degree of air dilution, aging, background levels, and sampling and analysis protocols differed among the various previous studies. The emission factors reported in the literature are consequently quite variable. For example, Brunnemann *et al.* (6) reported a NDMA concentration of 2.7 ng L^{-1} from 10 smoked cigarettes in a 400 L plastic glove box with "no air flow" which corresponds to an emission factor of 108 ng NDMA per cigarette assuming no air exchange. NDMA concentrations of 0.23 ng L^{-1} were reported for a 20-m^3 room with "no ventilation" from 100 smoked cigarettes, which corresponds to an emission factor of 46 ng of NDMA per cigarette assuming no air exchange. In another set of experiments reported by Brunnemann *et al.* (5), NDMA emissions from 15 to 80 cigarettes in a 20.87 m^3 experimental chamber averaged 225 ng per cigarette. These emission factors are all lower than the average NDMA emission factor that we measured for the six commercial brands of 565 ng per cigarette.

A sidestream emission factor of 372 ng per cigarette reported for NDMA for the 1R4F cigarette (11) is only slightly lower (16%) than the emission factor that we measured for ETS. However, the same study reported a sidestream emission factor of 179 ng per cigarette for NPYR for the 1R4F cigarette, compared to our ETS value of 98 ng per cigarette. There is some potential for depositional losses of NPYR because of its lower vapor pressure at room temperature (0.72 mm Hg) compared to NDMA (2.7 mm Hg). Therefore, we hypothesize that the lower value measured for ETS, compared to SS, could be due to some wall deposition in the environmental chamber during the 4.5 hour experiment.

Indoor Air Exposures to VNA from ETS

The average emission factors for the two VNA were used in combination with a time-dependent mass balance model to estimate indoor concentrations of these compounds from ETS for a residential and an office scenario. The input variables for the scenarios were selected to be representative of "average" rather than extreme conditions. Modeled indoor concentrations of NDMA and NPYR were then compared to those measured in other indoor settings and outdoor air.

For the residential scenario, we used average values from a recent field study of indoor aerosols in Suffolk County, NY (Leaderer *et al.*, 26). The average house volume was 352 m³; the average air exchange rate was 0.58 h⁻¹; and an average of 16 cigarettes were smoked per day in each house. For this exercise, it was assumed that the cigarettes were smoked at a rate of 1 per hour during waking hours but that two cigarettes were smoked at 7 a.m., 10 a.m., noon, and 5 p.m. The average indoor VNA concentrations were calculated for a 7-day period. The estimated average VNA concentrations were 2.0 ng m⁻³ and 0.4 ng m⁻³ for NDMA and NPYR respectively. The estimated indoor NDMA concentration is about 14 % of the unit risk value (one cancer per million) of 14 ng m⁻³ assigned by the U.S. EPA (27).

For the office scenario, we assumed a small office with a total volume of 1,059 m³ and 16 occupants, with 20 % smokers, each smoking 2 cigarettes per hour. An air exchange rate of 0.51 h⁻¹, based on the ASHRAE standard of 20 cfm of outside air per occupant (28), was used for the daytime working hours and a value of 0.41 h⁻¹ (29) was used for the remainder of each day. The volume of the office space was based on the average floor area of 70 small offices (30) and an assumed ceiling height of 3 m³. The smoking rate was based on data reported by Repace and Lowery (31). Estimated average concentrations over a 40-hour week were 5.0 ng m⁻³ and 1.0 ng m⁻³ for NDMA and NPYR, respectively.

We could find only one report of the measurement of NDMA in a residence (8) for comparison to the modeled concentrations for the residential scenario, and the concentration was reported as being less than the lower limit of detection, 17 ng m⁻³. There have been two recent reports of measurements of VNA in office settings, although the air exchange rates were not reported (7, 8). These are compared to the modeled concentrations for our office scenario in Table 4. The concentration reported by Stehlik *et al* (7), based on a sample collected over 2 hours, was considerably higher than the estimated concentration for our office scenario. However, the smoking rate was higher and the volume of the room was smaller than for our scenario. If we use their smoking rate and room volume in a mass balance model with an assumed ventilation rate of 2.9 h⁻¹ (to meet the ASHRAE Standard) and our emission factor, an average indoor concentration of NDMA of 37 ng m⁻³ is estimated for the 8-hour workday (excluding the lunch hour). This concentration is close to that actually measured by Stehlik *et al.*, and suggests that the emission factors were consistent.

Klus *et al.* (8) reported VNA concentrations for an 84 m³ office and smoking rates of 11 and 18 cigarettes in 2 hours (Table 4). We have used their room volume and smoking rate (11 cigarettes/2 hours, except during the noon hour) in combination with an assumed air exchange rate of 2.9 h⁻¹ in a time-dependent mass balance model and have compared the reported and predicted concentrations (Table 4). At 2.9 h⁻¹, the modeled concentrations of the VNA are 2 to 3 times higher than those measured; an air exchange rate of about 7 h⁻¹ would be required to produce a concentration for NDMA for an 8-hour work day that is consistent with the average of the reported measurements. This is probably an unrealistically high air exchange for an office which the authors report had no air mechanical ventilation. Alternatively, it is possible that the emission factors for the cigarettes used by Klus *et al.*, were considerably higher than those we measured.

The median concentration reported by Shah and Singh (32) for the available outdoor air measurements is 42 ng m⁻³ for NDMA. This concentration, however, is based on only 42 outdoor measurements, some of which were made in source-dominated outdoor areas, e.g., near chemical plants. Thus, this median concentration may be considerably higher than one based on more representative sampling of outdoor air. The median NDMA outdoor air concentration is 21 and 8 times higher than those estimated for the two indoor scenarios with ETS. With heavier smoking rates and low air exchange rates, ETS would be account for a larger fraction of total exposure to the VNA.

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References:

- 1) Jenkins, P.L.; Phillips, T.J.; Hui, S.P. *Atmos. Environ.* **1992**, *26A*, 2141-2148.
- 2) Wiley, J.A.; Robinson, J.P.; Piazza, T.; Garrett, K.; Cirkseña, K.; Cheng, Y. T.; Martin, G. *Activity patterns of California Residents*. Contract No. A6-177-33. California Air Resource Board, Research Division: Sacramento, CA, 1991.
- 3) Ruhl, C.; Adams, J. D.; Hoffmann, D. *J. Anal. Toxicol.* **1980**, *4*, 255-259.
- 4) Brunnemann, K. D.; Yu, L.; Hoffmann, D. *Cancer Res.* **1977**, *37*, 3218-3222.
- 5) Brunnemann, K. D.; Fink, W.; Moser, F. *Oncology*, **1980**, *37*, 217-222.
- 6) Brunnemann, K. D.; Hoffmann, D. In: *Environmental Aspects of N-nitrosocompounds* (IARC No. 19), Walker, E.; Griçute, L.; Castegnaro, M.; Lyle, R. (Eds), International Agency for Research on Cancer: Lyon, France, 1978; pp 343-356.
- 7) Stehlik, G.; Richter, O.; Altman, H. *Ecotoxicol. Environ. Saftey.* **1982**, *6*, 495-500.
- 8) Klus, H.; Begutter, H.; Ball, M.; Introp, M. In: *Proceedings of the 4th International Conference on Indoor Air Quality and Climate*, Seifert, B.; Esdorn, H.; Fischer, M.; Ruden, H.; Wegner, J. (Eds), Indoor Air'87 Vol. 2, Institute for Water, Soil and Air Hygiene: Berlin, 1987; pp 137-141.
- 9) Klus, H.; Begutter, H.; Scherer, G.; Tricker, A.; Adlkofer, F. *Indoor Environ.* **1992**, *1*, 348-350.
- 10) Tricker, A.R.; Klus, H.; Begutter, H.; Scherer, G.; Adlkofer, F. *Proceedings of Indoor Air '93*, **1993**, *3*, 47-52.
- 11) Caldwell, W. S.; Conner, J. M. *J. Assoc. Off. Anal. Chem.* **1990**, *73*, 783-789.
- 12) Chamberlain, W.J.; Arrendale, R.F. *J. Chromatogr.* **1982**, *234*, 478-481.
- 13) Pierce, J.P.; Goodman, J.; Gilpin, E.; Berry, C. *Technical Report on Analytical Methods and Approaches Used in the Tobacco Use in California, 1990-1991*. Department of Health Services: Sacramento, CA, 1992.
- 14) Chortyk, O.T.; Schlotzhauer, W.S. *J. Anal. Toxicol.* **1989**, *13*, 129-134.
- 15) Hecht, S. S.; Adams, J. D.; Hoffmann, D. In: *Environmental Carcinogens Selected Methods of Analysis, N-Nitroso Compounds* (IARC No 45) Egan, H.; Preussmann, R.; O'Neill, I. K.; Eisenbrand, G.; Spiegelhalder, B.; Bartsch, H. (Eds), International Agency for Research on Cancer: Lyon, France, 1983; pp 93-101.
- 16) Mirvish, S. S.; Wallcave, L.; Eagen, M.; Shubik, P. *Science* **1972**, *177*, 65-68.
- 17) Fine, D. H.; Rounbehler, D. P.; Belcher, N.M.; Epstein, S.S. *Science* **1976**, *192*, 1328-1330.
- 18) Cucco, J.A. and Brown, P.R. *J. Chromatogr.* **1981**, *213*, 253-263.

- 19) Rounbehler, D.P.; Reish, J.; Fine, D.H. *Food Cosmet. Toxicol.* **1980**, *18*, 147-151.
- 20) Fine D.H.; Rounbehler, D.P.; Goff U. In: *Environmental Carcinogens Methods of Analysis and Exposure Measurement* (IARC No 109), Seifert, B.; Van de Wiel, H.J.; Dodet, B.; O'Neill, I. K. (Eds), International Agency for Research on Cancer: Lyon, France, 1993;. pp 269-274.
- 21) Rounbehler, D.P.; Reish, J.W.; Coombs, J.R.; Fine, D.H. *Anal. Chem.* **1980**, *52*, 273-276.
- 22) Thermedics Detection, Inc., Analytical Instruments Division, Waltham, MA. Personal communication.
- 23) Daisey, J.M.; Mahanama, K.R.R.; Hodgson, A.T. *Toxic Volatile Organic Compounds in Environmental Tobacco Smoke: Emission Factors for Modeling Exposures of California Populations*. Contract No. A133-186. California Air Resource Board, Research Division: Sacramento, CA, 1994.
- 24) Burton, H. R.; Dye, N.K.; Bush, L.P. *J. Agric. Food Chem.* **1992**, *40*, 1050-1055.
- 25) Brunnemann, K.D.; Masaryk, J.; Hoffmann, D. *J. Agric. Food Chem.* **1983**, *31*, 1221-1224.
- 26) Leaderer, B. P.; Koutrakis, P.; Briggs, S.L.K.; Rizzuto, J. *Indoor Air.* **1983**, *4*, 23-34.
- 27) Jones, M. Information on Substances for Review as Toxic Air Contaminants. California Air Resource Board, Stationary Source Division: Sacramento, CA, 1989.
- 28) American Society of Heating, Refrigerating and Air-conditioning Engineers, Inc. 1989. ASHRAE Standard 62-1989, "Ventilation for Acceptable Indoor Air Quality," Atlanta, GA.
- 29) Grot, R.A.; Persily, A.K. In: *Measured Air Leakage of Buildings*. (ASTM STP 904) Terschel, H.R.; Lagus, P.L.; (Eds), American Society for Testing and Materials: Philadelphia, PA, 1986;. pp 151-183.
- 30) Akbari, H.; Eto, J.; Turiel, I.; Heinemeier, K.; Lebot, K.; Norman, B; Riner, L. *Integrated estimation of commercial sector end-use load shapes and energy use intensities*. UER-230, LBL-27512, Lawrence Berkeley Laboratory, Berkeley, CA,. 1989.
- 31) Repace, J.L.; Lowery, A.H. *Science.* **1980**, *208*, 464-472.
- 32) Shah, J.J.; Singh, H.B. *Environ. Sci. Technol.* **1988**, *22*, 1381-1388.

Table 1. Percent Recovery of Spiked VNA from Different Sampling Media.

Spiked VNA	Percent Recovery \pm Standard Deviation ^a	
	Thermosorb/N ^b	Impinger ^c
N-Nitrosodimethylamine	93 \pm 2	81 \pm 5
N-Nitrosodiethylamine	95 \pm 7	93 \pm 3
N-Nitrosopyrrolidine	103 \pm 4	91 \pm 3
N-Nitrosomorpholine	94 \pm 5	91 \pm 4
Mean \pm Standard Deviation	96 \pm 5	89 \pm 4

^a n = 5 samples

^b 114 ng of each compound was used for spiking

^c 95 ng of each compound was used for spiking

Table 2. Comparison of Two Sampling Methods for VNA in ETS.

Trial No.	ng VNA per Cigarette			
	N-Nitrosodimethylamine		N-Nitrosopyrrolidine	
	Cartridge	Impingers	Cartridge	Impingers
1	592	548	135	149
2	573	563	158	137
3	578	542	133	150
Mean	581	551	142	145
Std. Dev.	9.7	10.9	13.9	7.4
C. V. % ^a	2%	2%	10%	5%

^a C. V. = Coefficient of Variation = [Std. Dev X 100] / Average

Table 3. VNA Emission Factors for ETS from Six Commercial Cigarettes and Kentucky Reference Cigarette 1R4F

Cigarette	Description	Standard Length, cm ^a	Mass of tobacco per unit length, mg cm ^{-1b}	Emission Factor, ng VNA per cigarette ^c		Emission Factor, ng VNA per mg of tobacco ^d	
				NDMA	NPYR	NDMA	NPYR
A	Filtered	53	115.5	498	85	0.81	0.14
A ^e	Filtered	53	115.5	503	86	0.82	0.14
B	Filtered, light	49	117.1	572	105	1.01	0.19
C	Non-filtered	46	116.9	477	81	0.90	0.15
D	Filtered	56	113.7	447	100	0.70	0.16
E	Filtered, mentholated	65	123.4	750	135	0.96	0.17
F	Filtered, mentholated	64	113.0	645	118	0.89	0.16
1R4F	Filtered	48	135.0	449	100	0.69	0.15
1R4F ^e	Filtered	48	135.0	439	95	0.68	0.15
Mean ^f				565	104	0.88	0.16
Std. Dev. ^f				115	20	0.11	0.02
C. V. % ^g				20%	20%	12%	10%

^a Standard length in cm = [Length - (Filter over wrap + 0.03)]; for non-filter [Length - 0.23]

^b Mass per unit length = Average value from 6 cigarettes, butts were not included.

^c ng per cigarette = ng of VNA x standard length/actual smoked length.

^d ng per mg of tobacco = ng of VNA from one mg of tobacco consumed.

^e Duplicate chamber experiment

^f 1R4F omitted; n = 6, average of duplicate measurements of cigarette A used in overall average

^g C. V.= Coefficient of Variation = (Std. Dev. X 100) /Average.

Table 4. Comparison of Modeled and Measured Concentrations of VNA in Indoor and Outdoor Air

Scenario	Room/Bldg Volume, m ³	Smoking Rate	Air Exchange	Concentration, ng m ⁻³	
				<u>NDMA</u>	<u>NPYR</u>
Modeled, Residential, 1 smoker, week-long average (This study)	352	16 cig in 24 hr	0.58 h ⁻¹	2	0.4
Modeled, Small Office, 16 occupants, 4 smokers, 2 cigarettes per hour, 40-hr work week average (This study)	1059	6 cig per hr	0.41h ⁻¹	5	0.9
Measured, Office with smokers, closed windows (Stehlik, <i>et al.</i> , 1982)	70	27 cig in 2 hr	NA ^a	30	-
Modeled, Office with smokers, closed windows (Based on Stehlik, <i>et al.</i> , 1982, with assumed air exchange rate) ^b	70	27 cig in 2 hr	2.9 h ⁻¹	37.0 ^c	6.8 ^c
16 Measured, Office, controlled conditions (Klus, <i>et al.</i> , 1987)	84	11 cig in 2 hr	NA ^a	4.0	5.7
		11 cig in 2 hr		7.5	4.0
		11 cig in 2 hr		4.8	3.5
		18 cig in 2 hr		13.2	4.9
Modeled, Office, controlled conditions (Based on Klus, <i>et al.</i> , 1987, with assumed air exchange rate) ^b	84	11 cig in 2 hr	2.9 h ⁻¹	11.4 ^c	2.1 ^c
Measured outdoor air, 42 data points, remote, rural, suburban, urban, and source-dominated (Shah and Singh, 1988)	-	-	-	42 ^d	NA

^a NA = not available

^b Assuming NDMA and NPYR emissions factors measured in this study

^c Average for 8-hour workday (excludes lunch hour)

^d Median concentration

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