Note on Ethene and Other Low-Molecular Weight Hydrocarbons in Environmental Tobacco Smoke

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Levels of ethene and propene, together with those of some other light hydrocarbons (propane, butane, isobutane and ethyne), have been measured under realistic conditions in environmental tobacco smoke (ETS) as a step towards the elucidation of the sources of 2-hydroxyethyl and 2-hydroxypropyl adducts of hemoglobin observed in non-smokers. These adducts may reflect in vivo doses of carcinogenic epoxides that are metabolites of the respective alkenes. The data show that 2.0 mg ethene, 1.4 mg propene, and 0.7 mg propane together with smaller amounts of butane, isobutane and ethyne are released per cigarette smoked (0.66 g tobacco) of a common Swedish brand. The alkenes in ETS should be considered as contributing factors to a risk of systemic cancer from passive smoking. With regard to alkene intake, even a relatively mild exposure to ETS (2 cigarettes per h for 5 h per day in a 33 m² room with one air change per hour is estimated to correspond to the active smoking of about one cigarette per day.

Monitoring of hemoglobin (Hb) of adducts in humans and other mammals has revealed the occurrence of background levels of 2-hydroxyethylated and 2-hydroxypropylated amino acids (histidine and N-terminal valine) in individuals without known exposure. 1–4 These adducts may be formed via ethylene oxide 5,6 and propylene oxide, 7 respectively, as shown by raised levels in samples from persons with occupational exposure to these epoxides. Ethene and propene – of which ethylene oxide 8–11 and propylene oxide, 12 respectively, are the main primary metabolites – are generally formed during the combustion of organic matter and occur therefore as pollutants in urban air 13–15 and in tobacco smoke. 16 In agreement with this, Hb from cigarette smokers showed raised hydroxyethylation levels as compared with Hb from non-smokers, ethene in the mainstream smoke (about 0.25 mg per cigarette 17) being the most probable source. Furthermore, owing to production by terrestrial and marine organisms, ethene occurs in low concentrations (0.1–1 ppb) as a ubiquitous component of air. 14 Endogenous production of ethene in mammalian tissues (Refs. 13, 17, 18) should also be considered in the total budget of hydroxyethylations of human macromolecules.

Although a considerable proportion of the average background level in humans – about 100 pmol g⁻¹ Hb – of hydroxyethylvaline (HOEtVal) is due to raised levels in tobacco smokers, there is also a background level observed in non-smokers (range 10–100 pmol g⁻¹ Hb). 17,18 2-Hydroxypropylvaline (HOPrVal) also occurs in Hb from non-smokers although in smaller amounts than HOEtVal.

Clarification of the role of ambient alkenes in the formation of HOEtVal and HOPrVal in non-smokers contributes to the risk assessment of urban air pollution and of environmental tobacco smoke (ETS) (passive smoking), especially with

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† Abbreviations: Hb, hemoglobin; HOEtVal, N-(2-hydroxyethyl)valine; HOPrVal, N-(2-hydroxypropyl)valine; ETS, environmental tobacco smoke; MS, mainstream smoke; SS, sidestream smoke; EO, ethylene oxide; PO, propylene oxide; ppnm, ppm-hour.
regard to the relative importance of gaseous components in these mixed pollutions. Because of urban–rural differences in the prevalence and mode of tobacco smoking, this source of air pollutants should be considered also in studies where the aim is restricted to risk assessment of urban air pollution.

No reports on the measurement of the amounts of ethene and propene in sidestream smoke (SS) have been found in the literature. As a step towards the clarification of the origin of the background levels of light 2-hydroxyalkyl adducts – and of associated risks – indoor concentrations of these alkenes and, simultaneously, of some other hydrocarbons (ethyne, propane, butane and isobutane) were determined as a function of cigarette smoking. A method developed for automatic analysis of light olefins in urban air was used for the determination of concentrations.

Average hydrocarbon emission per smoked cigarette was determined by fitting a reasonable mathematical model to data from both intermittent and continuous smoking in an office.

**Experimental**

**Experimental design.** Four experiments (I–IV) were carried out in which the concentrations of the studied hydrocarbons were measured in an office of volume 39.3 m³ in which two persons smoked filter cigarettes of a common Swedish brand.

The smoking, ventilation and air-mixing conditions were varied according to Table 1. In experiments I, III and IV, the normal ventilation system of the building was used, while in II it was shut off and window frames were sealed. In experiments I and II, the air mixing factor was probably close to 1, but in experiments III and IV it was more normal. In experiments I, II and IV, the two persons smoked by turns, so that one cigarette was burning continuously; in experiment III, a normal ETS exposure situation was imitated, no, one or two cigarettes being smoked at any moment. The average smoking time per cigarette was 6.2 min, 0.66 g tobacco per cigarette being smoked (5 mm butt length).

The concentrations of ethene, propene, propane, butane, isobutane and ethyne in the air were determined over 2 min every 12 min, including three measurements made before smoking was commenced and three measurements after cessation of smoking. In experiment III, the analysis was limited to ethene and in experiment IV, concentrations of ethene, propene and propane were measured.

**Chemical analysis.** The analytical method used was based on an enrichment step using a solid sorbent and subsequent thermal desorption for gas-chromatographic analysis of the individual hydrocarbons.

For sampling of the air in the experimental room a portion of air was allowed to pass continuously at a rate of 750 ml min⁻¹ through a Teflon tube (7 m×5 mm i.d., 0.4 mm thickness) to the gas chromatograph (Shimadzu, GC MINI 3). The hold-up time in the Teflon tube was 11 s. From the Teflon tube, a sample of 80 ml was taken by means of pumping at 40 ml min⁻¹ through the

<table>
<thead>
<tr>
<th>Expt. No.</th>
<th>Ventilation</th>
<th>Air mixing</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>On (ca. 5 air changes per h)</td>
<td>Good (2 strong fans)</td>
<td>One cigarette continuously for 53 min (0.16 cig. min⁻¹)</td>
</tr>
<tr>
<td>II</td>
<td>Off (0)</td>
<td>= I</td>
<td>One cigarette continuously for 44 min (0.17 cig. min⁻¹)</td>
</tr>
<tr>
<td>III</td>
<td>On (= I)</td>
<td>Moderate (1 weak fan)</td>
<td>Individually during 86 min (in all 10.3 cigs.)</td>
</tr>
<tr>
<td>IV</td>
<td>On (= I)</td>
<td>= III</td>
<td>Continuously for 48 min (0.15 cig. min⁻¹)</td>
</tr>
</tbody>
</table>
solid sorbent (molecular sieve 13X, 40–60 mesh; Alltech, Deerfield, IL, USA) at ambient temperature. The sorbent was packed into a thin-walled nickel tube, which was connected to the chromatographic column via a 6-port valve. Heat-desorption of the sample was on-line with the column, over a period of 2 min, nitrogen being used as the carrier gas (25 ml min⁻¹). The column (stainless steel 5 m × 2 mm i.d.) was packed with activated alumina (80–100 mesh, Alltech) and the oven temperature was 180°C. Quantitation of the compounds was achieved by means of a flame ionization detector (FID). Data recording and peak processing were carried out with an integrator (HP 3392 A).

For quantitation, a standard of ethene was used (Alfax AB, Malmö, Sweden), bottled and dissolved in nitrogen gas, the concentration of the ethene being adjusted to 9.2 ± 0.5 ppm (by volume). From this standard, a small volume (0.5 ml) was withdrawn with a gas-tight syringe and analysed in the same manner as the samples. The other hydrocarbons were identified using qualitative standards and quantified using response factors relative to ethene, obtained from literature data.²⁷,²⁸ The concentration of the primary ethene standard was confirmed by using a fresh butane standard, which was prepared by successive dilutions of 100% butane (Alfax AB).

Data analysis. Under conditions of good air mixing, the variation in the concentration, C, of a hydrocarbon may be described by eqn. (1)

\[
\frac{dC}{dt} = \frac{na}{V} - kC
\]  

(1)

where \( n \) = number of cigarettes being smoked at time \( t \) (\( n = 0,1,2 \)); \( a \) = amount of the measured hydrocarbon released per min per cigarette smoked [(mg min⁻¹) cig⁻¹ if \( C \) is given in mg m⁻³]; \( V \) = volume of room (m³); \( k \) = rate of air change (min⁻¹).

Data from the experiments were fitted, using a non-linear least-squares regression method, to the function given in eqn. (2), which is the formal solution of (1). \( C(0) \) is the background level, which was determined separately by measurements made before the commencement of smoking. Fitting was performed by using the program MLAB.²⁹

\[
C(t) = a \exp(-kt) \int_0^t n(u) \exp(ku)du + C(0)
\]  

(2)

Results

Observed and calculated variations in the air concentrations of ethene and propene in experiments I and II are shown in Figs. 1 and 2, and corresponding data for ethene in experiment III are shown in Fig. 3. Estimated hydrocarbon emissions per cigarette for experiments I–IV are given in Table 2. The effective rate of ventilation calculated from eqn. (2) was 0.09 min⁻¹ in experiments III and IV.

Discussion

Hydrocarbon emission in ETS. Since small fractions of inhaled amounts of ethene,⁶–¹¹ propene,¹² and, with all probability, also of the other hydrocarbons, are metabolized and thus not re-exhaled, the figures in Table 2 are slightly lower than the total amounts in MS + SS.

It should be stressed that the aim of the present study was to measure air concentrations of low molecular-weight alkenes in ETS under practical conditions. The values in Table 2 are therefore not directly comparable with analytical data for components in MS and SS from cigarettes machine-smoked under standard conditions.

We believe that the conditions in experiments I and II were as close as possible to the postulated model (1), which can be seen from the low stan-

![Fig. 1. Observed (symbols) and fitted concentrations of ethene and propene in experiment I. The average backgrounds (ethene 2.7 ppb, propene 1.6 ppb) have been subtracted.](image-url)
standard errors of the estimates and from the agreement between the experiments (Table 2). The slightly higher values obtained in experiments III and IV probably result from insufficient air mixing leading to inhomogeneous distribution in the room, also at steady state. This effect cannot, however, be described in terms of an empirically determined mixing factor, \( m \), which is supposed to affect only the time taken to reach a homogeneous steady state. A correct model for non-ideal mixing should take into account the positions in the room of the source and sampling points as well as directions and forces of air flows.

To our knowledge, the SS/MS ratio for ethene has not been previously determined. Published values for ethene in MS correspond to the range 0.2–0.3 mg per cigarette with one value at about 0.6 mg per cigarette (in these calculations 1 mol% or vol.% was assumed to correspond to 0.16 mmol; cf. Refs. 30, 31). If the MS content of ethene is 0.25 mg per cigarette, the SS/MS ratio would be ca. 7, i.e. a relatively high value compared with those for other light hydrocarbons (e.g. methane: ca. 3; 32 from such comparisons NRCC estimates ca. 1 mg ethene to be released into the environment per cigarette smoked, but recognizes that this may be an underestimation).

For propene + propane, Brunemann et al., 32,47 have given a ratio of 4.1, with 0.5 mg per cigarette in the MS. These values would correspond to a release in to the ETS, of 4.1×0.5 mg (in SS) + ca. 0.8×0.5 mg (re-exhaled) = 2.45 mg per smoked cigarette, in acceptable agreement with the sum, 2.1 mg per cigarette, for these components in Table 2 (Experiments I, II).

**Biological aspects.** Important biological aspects of the occurrence of alkenes in ETS concern the contributions of these compounds to the observed background levels of 2-hydroxyalkyl adducts\(^{14}\) and to the risk of cancer from passive smoking. The 2–4 carbon alkanes are not known to be genotoxic, although small effects of carbonyl intermediates cannot be excluded. Metabolism of ethyne (acetylene) proceeds via acetate; no Hb adducts from an intermediate epoxide were seen in a preliminary study (unpublished data).

An estimation of the contributions to background adduct levels requires knowledge of exposure doses of alkenes and of their metabolism in humans. It can be shown that, although concentration will vary during intermittent smoking, the exposure dose [time integral of \( C \) in eqn. (1)] corresponds to

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**Table 1.** Amounts, with S. E., of the studied hydrocarbons released to the environment per cigarette smoked (0.66 g tobacco), calculated from eqn. (2) fitted to data from experiments I–IV.

<table>
<thead>
<tr>
<th></th>
<th>I/mg</th>
<th>II/mg</th>
<th>III/mg</th>
<th>IV/mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethene</td>
<td>1.97(4)</td>
<td>1.93(1)</td>
<td>2.1(1)</td>
<td>2.4(2)</td>
</tr>
<tr>
<td>Propene</td>
<td>1.43(3)</td>
<td>1.41(1)</td>
<td>1.8(1)</td>
<td></td>
</tr>
<tr>
<td>Propane</td>
<td>0.70(2)</td>
<td>0.64(1)</td>
<td>0.96(7)</td>
<td></td>
</tr>
<tr>
<td>Butane</td>
<td>0.17(1)</td>
<td>0.17(1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isobutane</td>
<td>0.05(1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethyne</td>
<td>0.16(2)</td>
<td>0.13(1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Fig. 2.** Observed (symbols) and fitted concentrations of ethene and propene in experiment II.

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**Fig. 3.** Observed (asterisks) and fitted concentrations of ethene in experiment III. The average background (3 ppb) has been subtracted. Duration of smoking and no. of cigarettes are shown above the time axis (----).
\[
D_{\text{exp}} = \int C(t)dt = \frac{(\text{emitted amount cig.}^{-1}) \times (\text{no. of cigarettes})}{k' V}
\]

In the absence of precise data for the parameters in (3), a rough estimation of the order of magnitude of a mean value may be made. Within the work of the Swedish Cancer Committee,\textsuperscript{33} the quantitative reasonableness of the excess cancer risk indicated in Hiyaruma’s\textsuperscript{34} epidemiological study of non-smoking Japanese women with smoking husbands, was studied\textsuperscript{35} using an estimation of the cancer risk from assumed exposure doses of ETS. In this calculation, an average daily exposure dose was assumed to correspond to 2 cigarettes h\textsuperscript{-1} for 5 h, \( V = 33 \text{ m}^3 \), \( k' = \text{one effective air change per h} \). This moderate exposure may just as well be used as a measure of the order of magnitude of an average daily exposure dose in Swedish homes. The daily exposure dose of ethene estimated by the insertion of these parameter values into eqn. (3) amounts, accordingly, to 0.6 mg m\textsuperscript{-3} h\textsuperscript{-1} (= 0.55 ppmh).

At low exposure levels, the inhalation of 1 mg ethene per kg body weight gives rise to approximately the same tissue dose\textsuperscript{36} of ethylene oxide (EO) in mice (experiments with ethene\textsuperscript{10}), rats and hamsters (measurement of Hb adducts in animals exposed to automotive engine exhausts\textsuperscript{4}) and in humans. The latter was judged from the incremental level of HOEtVal in Hb from smokers, ca. 10 pmol g\textsuperscript{-1} Hb per cigarette per day,\textsuperscript{17,37} assuming that the inhaled amount of ethene is equal to the amount, ca. 0.25 mg,\textsuperscript{16} in the mainstream smoke (MS) from a cigarette.

The inhalation rate of a human adult at rest is about 0.5 m\textsuperscript{3} h\textsuperscript{-1}. In the exposure situation suggested above (\( D_{\text{exp}} = 0.6 \text{ mg m}^{-3} \text{ h} \)), ca. 0.3 mg ethene, i.e. approximately the amount in the MS from one cigarette, will be inhaled per day. This uptake rate is accordingly expected to give rise to a steady-state level of some 10 pmol HOEtVal g\textsuperscript{-1} Hb. From animal studies\textsuperscript{4,12} the simultaneous increment of HOPrVal is expected to be some five times lower.

Alkenes in ETS are accordingly expected to be essential contributors to observed background levels of HOEtVal and HOPrVal in humans. In an epidemiological pilot study aiming primarily at urban—rural differences this contribution was not detected [effect of passive smoking (0 ± 15) pmol HOEtVal g\textsuperscript{-1} Hb], evidently because of low reproducibility of the analytical method at low levels and because of variations in other sources of HOEtVal.\textsuperscript{19}

Both EO\textsuperscript{38–42} and PO\textsuperscript{38,42} have exhibited carcinogenic properties in animal tests, and raised cancer incidence has also been indicated in human populations with occupational exposure to EO.\textsuperscript{43} Since dose response curves for cancer initiators/mutagens should be considered as being linear,\textsuperscript{36} it is natural to consider also the metabolic precursors, ethene and propene, of the epoxides to be carcinogens, although, because of the saturation kinetics of the metabolic conversion,\textsuperscript{3,44,45} this is not detectable in regular long-term animal studies.\textsuperscript{46} A report on the estimated magnitude of the cancer risk from the alkenes awaits current dosimetric studies in humans.

Some comments do, however, seem to be justified at this stage. Under the conditions assumed, the estimated dose of ethene received by a passive smoker corresponds to that received in active smoking of about one cigarette per day, i.e. 10% of the dose of an average Swedish active smoker (10 cig. per day\textsuperscript{33,35}). This figure is in the range of that estimated for other gaseous components\textsuperscript{47} and is appreciably less than the cigarette equivalent of particulate components received by passive smokers. One reason for this difference is the precipitation of particles leading to lower doses compared with those of gaseous components.\textsuperscript{26}

Doses of low molecular-weight epoxides are, based on animal experiments,\textsuperscript{10} expected to be equally distributed in the body. These components of ETS are therefore expected to give rise to systemic tumours rather than to the lung tumours studied in the first reports, among others that of Hiyaruma,\textsuperscript{34} on the risk of cancer from passive smoking. More recent epidemiological studies of passive smokers support this expectation by indicating an increased incidence of tumours at sites other than the respiratory tract (for a review see Ref. 47).

Acknowledgements. Mrs. Beryl Holm is gratefully acknowledged for linguistic assistance in preparing this manuscript. The present study was supported financially by the National Swedish Environment Protection Board and the Bank of Sweden Tercentenary Foundation.
HYDROCARBONS IN TOBACCO SMOKE

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Received May 20, 1988.