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Determination of physiological levels of volatile organic compounds in blood using static headspace capillary gas chromatography with serial triple detection

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A static capillary gas chromatographic method using three different detectors [photoionization detector (PID), electron capture detector (ECD) and flame ionization detector (FID)] switched in series is presented for the determination of volatile organic compounds (VOCs) in sub μg l^{-1} levels. The method was applied for the analysis of selected environmentally and occupationally relevant non-halogenated and chlorinated aromatic hydrocarbons (*e.g.*, benzene, toluene, xylenes, dichlorobenzenes) as well as chlorinated aliphatic hydrocarbons (*e.g.*, trichloroethene, tetrachloroethene) in blood samples. Detailed investigations, in respect to the figures of merit were carried out. For most of the selected VOCs detection limits (calculated as the three-fold standard deviation of low level calibration standards) in the range from 26 (benzene) to 67 ng l^{-1} (*m/p*-xylene) were achieved which are comparable with those reported for dynamic headspace techniques in combination with mass spectrometric detection. For the individual VOCs the within-series precision varied from 4 to 19% and the day-to-day precision from 11 to 28%. Regarding PID as well as FID the calibration graphs for all substances were linear up to at least 10 μg l^{-1} while the ECD response was linear up to concentrations of about 0.6 μg l^{-1} for the halogenated compounds. Our method is applicable for the quantitative determination of VOCs in blood in the occupationally as well as in the physiologically relevant (normal) concentration range.

Keywords: *Biological monitoring; volatile organic compounds; environmental concentrations; gas chromatography; headspace technique; photoionization detection*

Due to their wide use and their physico-chemical properties volatile organic compounds (VOCs) are widely distributed in the environment, at the workplace and at home. Their main sources are from their use as solvents in paints, adhesives, degreasers or related products and emissions from combustion processes including those from automobiles and cigarette smoking. Vapours of VOCs are readily absorbed by humans mainly *via* the lungs and skin, in some cases the oral absorption may also be of considerable importance. The individual exposure of a person to VOCs and the resulting health risk can thus only be evaluated by the determination of the internal exposure. Useful parameters for internal exposure assessment are the determination of the VOCs in blood and of their metabolites in urine.

The advantages of the gas chromatographic (GC) VOC determination in blood are well known and documented.[1–4] Due to their volatility the parent compounds can be easily separated by headspace techniques and additional sample preparation steps are generally not necessary. The use of sensitive and selective detectors, if necessary in combination with dynamic headspace techniques which allow the simultaneous enrichment of the VOCs, permits the accurate determination down to the lower ng l^{-1} level. Ashley *et al.*,[1] for example, reported detection limits for the determination of benzene, toluene and *o*-, *m*-, and *p*-xylene ranging between 19 and 38 ng l^{-1} using purge and trap GC–MS. Jermann *et al.*[3] who used the dynamic headspace technique in combination with GC–flame ionization detection (FID) found detection limits of 15 and 20 ng l^{-1}, respectively, for benzene and toluene in blood. Benzene levels in venous blood samples of 130 children ranged between < 15 and 350 ng l^{-1}, while toluene ranged between 130 and 3530 ng l^{-1}.[3] Brugnone *et al.*[5] determined blood benzene levels in 293 non-smokers and 138 smokers by dynamic headspace GC–MS. They found benzene levels between 7 and 924 ng l^{-1} in non-smokers and between 7 and 2241 ng l^{-1} in smokers.

The determination of urinary VOC metabolites is another approach for individual exposure assessment. It has, in principle, some advantages over the determination of the parent compounds such as the longer half-life of the metabolites and the lower risk of contamination and losses during sample collection, storage and preparation. At the same time it offers the possibility to apply a non-invasive sample collection technique. Though intensively used for the routine monitoring of occupationally exposed workers, there are only few data from the field of environmental exposure. In the past years the main field of research has been the development of analytical procedures for the determination of the minor benzene metabolites *trans*,*trans*-muconic acid and *S*-phenylmercapturic acid.[6–9] However, more sophisticated analytical procedures and a multi-step sample preparation including separation, enrichment, derivatization and clean-up are required for the assessment of the environmental concentration range making this approach less suitable for routine monitoring than the direct determination in blood. Additionally, the specifity of the urinary metabolites is not sufficiently proven. In a recent paper, for example, Ruppert *et al.*[7] showed that the specifity of *trans*,-*trans*-muconic acid as a biomarker for low-level benzene exposure is limited because it is also a metabolite of sorbic acid being a widely used food preservative. Up to now the determination of the urinary metabolites is not a satisfactory alternative to the direct determination of the parent compounds in blood.

Several instrumental variations are described for the low-level VOC determinations in blood. These include different sampling techniques, such as static[10,11] or dynamic headspace[3–5,12] and the purge and trap technique[1, 2] on the one hand, and different detector types and combinations like MS,[1,4,5] ion trap detector (ITD),[2] photoionization detector (PID),[10,11] FID[3,12] and electron capture detector (ECD)[13] on the other hand.

In the analysis of minor amounts of VOCs in complex matrices selective detectors such as the halogen-selective ECD

and mass selective detectors should be used. A promising alternative may become the PID because of its higher sensitivity and selectivity towards aromatic compounds and C=C-double bonds in unsaturated compounds. The selectivity of this type of detector can be additionally varied by changing the radiation sources, which are available with different photon energies. Additionally, the PID as well as the ECD are non-destructive detectors and can be thus switched in series with other types of detectors. The in-series combination of different types of detectors has several advantages. Different sensitivities and selectivities of the detectors towards different classes of VOCs can be utilized within a single run. The constant ratios of the peak areas of a particular compound referring to two different detectors can be used as additional substance specific parameters and represent a criterion for the purity of peaks. The different linear dynamic ranges of the detectors can be utilized for the quantification in a wider concentration range. Compared with a parallel combination[14] of two different detectors, an arrangement in series has the advantage, especially for trace analysis, that the whole sample passes through all detectors resulting in a higher sensitivity and in a better reproducibility. In this paper a procedure is described for the sensitive and specific simultaneous determination of different classes of VOCs using static headspace capillary gas chromatography and an in-series combination of three detectors of different selectivity (PID–ECD–FID). The described procedure permits the routine monitoring of these VOCs in human blood samples in the occupational as well as in the environmental (normal) concentration range. Besides the toxicological relevance the selection of the individual VOCs (see Experimental) included in this investigation is based on previous studies[1–3,15] in which these compounds have been detected in human blood samples.

Experimental

Instrumentation

The investigations were carried out with a gas chromatograph type 4160 equipped with a headspace autosampler type 250 (both Carlo Erba, Milan, Italy). To avoid undesired changes of the blood samples (coagulation) caused by thermal stress within the heated autosampler, an additional self-made construction was attached to the autosampler, which permitted constant incubation rates of 6 h at 65 °C for each blood sample.

The gas chromatograph was equipped with a split/splitless injector including a septum purge and a 60 m DB-5 fused-silica capillary column (J&W Scientific, Folsom, CA, USA; thickness 0.25 μm; diameter 0.32 mm). The first part of the column (*ca.* 15 cm) was surrounded by a thermo-regulation chamber controlled by a multi function actuator MFA 515 (Carlo Erba). In order to trap and focus the compounds, the thermo-regulation chamber was cooled with liquid nitrogen during sample injection, while the split was closed. Then the split remained closed and the initial temperature was kept constant for a particular time (splitless time). The chamber was then heated rapidly to transfer the sample vapours quickly to the separation part of the column with the split being opened. The setting of the split and the splitless time was also controlled by the MFA 515. This system was equipped with a syringe purge which is active during sampling and injection in order to minimize the risk of contamination caused by ambient air during these operations.

The three different detectors, PID (UV source 10.2 eV, controller PI-52, HNU Systems, Newton, MA, USA), ECD (ECD-40, control-module ECD 4100, Carlo Erba) and the FID (FID-40, control-module EL 490, Carlo Erba), were combined in series. The PID and the ECD were coupled *via* an uncoated fused-silica transfer-line (length 30 cm, diameter 0.53 mm) whereas the FID was connected directly to the outlet of the ECD. The GC system is schematically shown in Fig. 1.

The parameters for the temperature program of the GC oven were set and controlled by a LT 410 programmer (Carlo Erba). Each detector was connected to an integrator for data aquisition and evaluation. The GC operation conditions are summarized in Table 1.

Sample collection

Venous blood samples were taken using disposable syringes and needles (10 ml, Sarstedt, Nümbrecht, Germany). To avoid contamination by organic solvents from conventional disinfectants, a 3% aqueous solution of hydrogen peroxide ('suprapure', Merck, Darmstadt, Germany, diluted with ultrapure water) was used for disinfection before puncture. The blood samples were immediately transferred into gas-tight glass vials (10 ml, first hydrolytic class, Zinsser Analytik, Frankfurt, Germany) containing 17.5 mg K_2-EDTA (puriss., Fluka, Buchs, Switzerland) per 10 ml of blood as anticoagulant which was cleaned before by heating at 150 °C for 12 h. The vials were

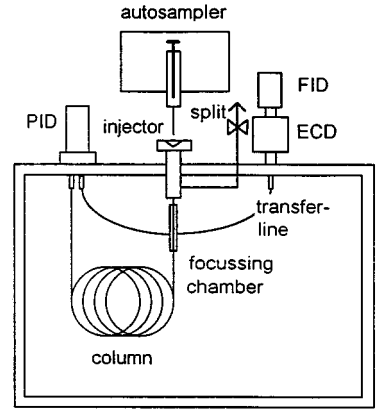

Fig. 1 Schematic diagram of instrumentation.

Table 1 Experimental conditions of the headspace autosampler, gas chromatograph, MFA515, and the three detectors (PID, ECD, FID)

HS sampler—	
Sample temperature	65 °C
Incubation time	6 h
Syringe temperature	80 °C
Injection volume	2.5 ml
GC—	
Carrier gas (N_2, ECD-grade)	Flow 1.5 ml min^{-1}
Septum purge	1.5 ml min^{-1}
Detector temperature	300 °C
Injector temperature	130 °C
Oven temperature profile:	38 °C for 10 min; 3° min^{-1} to 140 °C; 3 min hold, after cooling 7 min conditioning
Focussing (MFA 515)—	
Initial temperature	−75 °C
Splitless time	180 s
Final temperature	170 °C
PID—	
Lamp intensity	5 (relative range: 0–10)
Temperature	160 °C
Make-up gas (N_2)	20 ml min^{-1}
ECD—	
Mode	Constant current
Temperature	350 °C
Make-up gas (N_2)	30 ml min^{-1} (total)
FID—	
Detector gases	Air, 1.0 bar; H_2, 0.5 bar
Run time	60 min

then closed with caps containing silicon septa (Zinsser, Analytic, Frankfurt, Germany) and stored at +4 °C until analysis.

All handling of the blood samples was performed in a laminar flow cabin equipped with an activated charcoal filter.

Reagents and standard solutions

In order to reduce the analytical blank all used glassware, vials and silicon septa were washed with deionizised water and subsequently heated at 150 °C overnight.

The VOCs used for the calibration standards were obtained from several manufacturers in the highest available purity. Stock solutions were prepared in methanol ('for organic residue analysis', Mallinckrodt Baker, Griesheim, Germany). Four different stock solutions containing different classes of VOCs (1, non-halogenated aromatic hydrocarbons; 2, halogenated aliphatic compounds; 3, dichlorobenzenes; and 4, styrene) were used to avoid any chemical reaction of the components. These stock solutions (concentration of the substances about 40 mg l^{-1}) can be stored for at least six months at 4 °C. The calibration standards were prepared daily from the stock solutions by dilution with ultrapure water. The ultrapure water was prepared by cleaning with a commercially available water deionization system (Millipore, Eschborn, Germany) and additional purification using an UV-reactor (Gränzel, Karlsruhe, Germany). Blood of ram (GLD, Mülheim, Germany) was used for matrix-adapted calibration. Inside a laminar flow cabin headspace-vials are filled with 2 ml of blood (or ultrapure water, respectively) and 200 μl of standard solution and closed immediately.

The concentrations of the different calibration standards are summarized in Table 2. For the determination of the analytical blank analagous dilutions of pure methanol were made (S0).

Calibration and evaluation

The analytical blanks were determined using aqueous standards. The blank levels can originate from the methanol used for the stock solution, the glassware, the septa, ambient air or from the GC system. These blanks can not be eliminated completely for all compounds, but they can be minimized by careful handling of all analytical steps involved.

The calibration was carried out with standards in blood (ram) and ultrapure water with each calibration point being measured twice. The amounts of VOCs in the actual samples were calculated from the calibration slopes of the blood standards which were corrected for the analytical blank.

Table 2 Concentrations of the used calibration standards (μg l^{-1}), related to the volume of 2 ml blood or pure water, *m/p*-xylene 1 : 1

	S1	S5	S10	S20	S60	S100
Benzene	0.110	0.549	1.10	2.20	6.60	11.0
Toluene	0.108	0.542	1.08	2.17	6.50	10.8
m/p-Xylene	0.215	1.080	2.15	4.31	12.9	21.5
o-Xylene	0.110	0.550	1.10	2.20	6.60	11.0
Ethylbenzene	0.109	0.544	1.09	2.18	6.53	10.9
Styrene	0.114	0.569	1.14	2.28	6.83	11.4
1,3,5-Trimethylbenzene	0.109	0.544	1.09	2.18	6.53	10.9
1,1,1-Trichloroethane	0.131	0.656	1.31	2.62	7.87	13.1
Trichloroethene	0.147	0.735	1.47	2.94	8.82	14.7
Tetrachloroethene	0.162	0.812	1.62	3.25	9.74	16.2
Tetrachloromethane	0.199	0.994	1.99	3.98	11.9	19.9
1,2-Dichlorobenzene	0.165	0.825	1.65	3.30	9.90	16.5
1,3-Dichlorobenzene	0.161	0.806	1.61	3.23	9.68	16.1
1,4-Dichlorobenzene	0.183	0.913	1.83	3.65	11.0	18.3

Detection limits and quality control assesssment

The detection limits were calculated as the threefold standard deviation of replicate measurements (n = 9) of low level calibration standards (FID, S20; PID, S1; ECD, S1; dichlorobenzenes, S20; see Table 2).

The within-series precision and the day-to-day precision were investigated by replicate measurements (n = 5) of blood standards (S5, see Table 2). Regarding benzene and toluene the within-series precision was determined in another blood sample (blood spiked with 88 ng l^{-1} benzene and 87 ng l^{-1} toluene) which was analyzed tenfold.

All analyses were carried out under internal quality control conditions. According to the Commission for the investigation of Health Hazards of Chemical Compounds in the work Area of the German Science Foundation the therm 'internal quality control' is defined as follows: 'Internal quality control is the procedure of utilizing the results of only one laboratory for quality control purposes'. Thus an internal control sample was analyzed within each analytical series. Because control samples with known or certified VOC concentrations are not commercially available, they were prepared in our laboratory by pooling real samples which were stored in portions at +4 °C.

In the case of benzene, toluene, *o*-, *m*-, *p*-xylene, trichloroethene and tetrachloroethene external quality control was achieved by participation in an interlaboratory comparison program (German Society for Occupational and Environmental Medicine, Erlangen, Germany) including blood samples for the analysis of these VOCs in the occupationally relevant concentration range. The designated concentration of the blood samples included in the interlaboratory comparison and our result are compared in Table 3.

Optimization of the focussing temperature

The optimization was performed with aqueous VOC solutions using focussing temperatures between −1 °C and −150 °C. The optimum was obtained at a temperature of −75 °C. At temperatures lower than −75 °C the exact regulation of the temperature was not possible resulting in a deterioration of the reproducibility. Higher temperatures than −75 °C led to a considerable decrease of the peak areas.

Influence of the PID parameters

For examination of the influence of the PID parameters aqueous VOC standards were used again. The parameters (lamp intensity; temperature, make-up gas flow) were set to a high level (7; 200 °C; 45 ml min^{-1}) or a low level (2; 140 °C; 15 ml min^{-1}) in all possible combinations. The resulting signal-to-background ratios were used as measure of sensitivity.

Table 3 Results of the external quality control assessment; participation in an interlaboratory comparison program (German Society for Occupational and Environmental Medicine, Erlangen, Germany)

		Assigned value/μg l^{-1}		
Compound		Mean	Range (3σ)	Our result/ μg l^{-1}
Benzene	A	2.93	1.50–4.40	2.20
	B	5.88	3.20–8.50	4.90
Toluene	A	25.65	16.10–35.20	23.20
	B	248.71	175.40–322.0	220.0
m-Xylene	A	29.15	17.70–40.60	24.80
	B	307.19	219.70–394.70	264.0
Trichloroethene	A	16.35	8.90–23.80	10.90
	B	114.83	72.90–145.80	94.20
Tetrachloroethene	A	21.99	13.10–30.90	17.60
	B	154.57	109.90–199.20	64.20

The peak areas and thus the signal-to-background ratios were nearly unaffected by the PID temperature, but the variation of the other parameters had a significant influence. In the investigated range an inverse linear correlation between the make-up gas flow and sensitivity was found. If all other parameters were kept constant, the reduction of the make-up gas flow by a factor of three led to a threefold increase of the peak areas. An increase of the lamp intensity also resulted in elevated signal-to-background ratios, but the relation was found to be non-linear.

Furthermore the influence on the reproducibility (four replicates) and on the peak width was also taken into consideration. A significant effect on the peak width, especially an undesired broadening of the signals, did not occur in any of the combinations. The reproducibility expressed as relative standard deviation (RSD) seemed to be slightly better for higher lamp intensities and higher make-up gas flows. However, the reproducibility was in all tested combinations satisfactory (RSD < 10 %).

The in-series combination of the PID and the ECD (constant current mode) led to an increase of the basic ECD-frequency from 3 kHz (PID switched off) to 10 kHz (PID switched on) accompanied by a slight increase of the baseline noise. However, even if both detectors are operated simultaneously the ECD response remained in the acceptable range.

Results and discussion

The described GC system permits the separation and sensitive and reliable determination of all VOCs listed in Table 2. The in-series combination of three detectors with different selectivities makes it possible to determine each VOC with the optimal detector within a single run. Cryofocussing using liquid nitrogen resulted in an improvement of the detection limits by a factor of about 10.

The detection limits for the determination of these VOCs in blood and obtained with these three detectors are given in Table 4. Regarding benzene, toluene, xylenes and ethylbenzene detection limits obtained with static headspace GC and PID detection ranged between 26 and 67 ng l^{-1} and were thus between a factor of 14 and 37 better than those obtained with static headspace GC and FID detection. They are comparable with the detection limits which are reported for dynamic headspace techniques combined with FID,[3,12] MS[1] or ITD[2] detection. Our results are in good accordance with those of Kok and Ong[10] who determined benzene in human blood using static headspace GC with a detection limit of 50 ng l^{-1} (our detection limit: 26 ng l^{-1}).

Table 4 Detection limits (ng l^{-1}) for PID, ECD and FID

	Detection limit/ng l^{-1}		
Compound	PID	FID	ECD
Benzene	26	370	—
Toluene	45	640	—
m/p-Xylene	67	1520	—
o-Xylene	32	< DL*	—
Ethylbenzene	33	1210	—
Styrene	57	< DL	—
1,3,5-Trimethylbenzene	260	< DL	—
1,1,1-Trichloroethane	—	—	40
Trichloroethene	—	—	49
Tetrachloroethene	68	< DL	35
Tetrachloromethane	—	—	32
1,2-Dichlorobenzene	460	< DL	860
1,3-Dichlorobenzene	250	< DL	450
1,4-Dichlorobenzene	—	—	910

* DL is detection limit.

The simultaneous determination of benzene and toluene by static headspace GC and PID detection was also reported by Pekari *et al.*[11] These authors found that detection limits obtained with PID detection were by a factor of 10 better than those obtained with FID detection, which is in good accordance with our results. However, detection limits given by Pekari *et al.*[11] were 400 ng l^{-1} for both solvents and thus by a factor of about 10 worse than ours. However, Pekari *et al.* did not concentrate the analytes by cryofocussing.

Detection limits of the three dichlorobenzene isomers obtained with PID and ECD detection were comparable (see Table 4) and ranged between 250 and 460 ng l^{-1} for PID and between 450 and 919 for ECD detection. However, these detection limits, are all too high to enable detection of these compounds at environmental concentrations. A possible explanation for the relatively high detection limits of the dichlorobenzenes are their higher boiling points leading to lower equilibrium concentrations in the headspace. This may be also the explanation for the relatively high detection limit in the case of 1,3,5-trimethylbenzene (260 ng l^{-1}) having the highest boiling point of the investigated non-halogenated aromatics. An increase of the autosampler temperature to 80 °C in order to get higher headspace concentrations, turned out to be not appropriate because it led to an increase of the number of unknown peaks disturbing the chromatograms and to an increase of the amount of water vapour in the gas phase. A more suitable sample introduction technique for the analysis of higher boiling compounds may be the purge-and-trap or dynamic headspace technique.[1,2] Ashley *et al.*,[1] for example, reported a detection limit of 36 ng l^{-1} for 1,4-dichlorobenzene in blood. Detection limits for the three dichlorobenzene isomers using purge-and-trap GC–ITD are given by Dunemann and Hajimiragha[2] and ranged between 93 and 110 ng l^{-1}.

In order to check the influence of the above mentioned increased base frequency of the ECD occuring when the ECD and the PID are both operated simultaneously, the detection limits were also determined with the PID being switched off. In the case of 1,1,1-trichoroethane and trichloroethene the detection limits were found to be better by a factor of about 2, whereas those for tetrachloromethane and tetrachloroethene remained unchanged.

The linearities of the detector responses were checked in the concentration ranges covered by the six calibration standards given in Table 2. In both cases, PID and FID detection, the calibration graphs were linear over the examined range. For ECD detection the results were not uniform. The calibration graphs for the three dichlorobenzene isomers were also linear up to the calibration standard S100, whereas the response for the aliphatic halogenated compounds was linear only up to the calibration standards S5 (concentrations see Table 2). This finding can be explained by the greater number of halogen atoms in the molecules of these aliphatic halocarbons.

The within-series precision expressed as RSD of the measured peak areas ($n = 5$) for the spiked blood sample (S5) is given in Table 5. The RSDs were generally lower than 20%, for benzene and toluene with PID excellent RSDs of 6% and 4% were achieved. Due to the fact that this blood standard was spiked with relatively high VOC concentrations of about 500 ng l^{-1} (see Table 2), the determination of the within-series precision was repeated by analyzing aliquots ($n = 10$) of a blood sample spiked with 88 and 87 ng l^{-1} benzene and toluene, respectively. In this case RSDs of 17% for benzene and 16% for toluene were found. The results regarding the day-to-day precision are summarized in Table 6. As anticipated, the RSDs of the variation from day to day were higher than those for the variation within a series, but were nevertheless all in an acceptable range (11–28%). However, it has to be taken into consideration, that the day-to-day precision is not only influenced by the sample preparation and the instrumental

determination, but can also be affected by changes of the spiked blood during storage. The results for the day-to-day precision also confirm that the PID response is stable over a longer period of time (4 weeks) which is especially of importance in routine use.

Finally, as an important criterion for quality control an internal comparison with two other GC systems which are also used in our laboratory was carried out. Both reference systems are well established and have been successfully used for the determination of background VOC levels in blood. The first system represents the dynamic headspace (HS) technique combined with MS ion trap detection (dyn. HS–ITD)[16] and is the on-line version of a method which has already been described in detail in a former paper.[2] The second method is based also on the dynamic headspace (HS) technique, but the FID is used for detection (dyn. HS/ FID).[3] Both systems have similar detection limits for benzene, toluene and xylenes as the system described in this paper (stat. HS–PID). The comparison was carried out with animal blood samples spiked with benzene and toluene to final concentrations in blood of about 100 ng l^{-1}. The sample preparation, calibration and evaluation for all three systems were carried out under identical conditions (see Experimental). The determinations were performed simultaneously, which has the advantage that potential deviations are mainly a result of the different systems. Results (means and standard deviations of 10 replicate measurements) are summarized in Table 7. Taking into account the very low benzene and toluene concentrations and the complexity of the matrix, agreement between the results is satisfactory.

Table 5 Within-series precision (n = 5) of a spiked blood sample (S5), RSD in %

	Detection limit/ng l^{-1}		
Compound	PID	FID	ECD
Benzene	6	6*	—
Toluene	4	10*	—
m/p-Xylene	4	12*	—
o-Xylene	6	—	—
Ethylbenzene	13	19*	—
Styrene	14	—	—
1,3,5-Trimethylbenzene	15	—	—
1,1,1-Trichloroethane	—	—	14
Trichloroethene	—	—	4
Tetrachloroethene	11	—	12
Tetrachloromethane	—	—	9
1,2-Dichlorobenzene	17	—	9*
1,3-Dichlorobenzene	18	—	16
1,4-Dichlorobenzene	—	—	8*

* Spiked blood sample (S20).

Table 6 Day-to-day precision of spiked (S5) blood samples (n = 5), RSD in %

	Mean/ng l^{-1}	s/ng l^{-1}	RSD (%)
PID—			
Benzene	192	54	28
Toluene	276	57	21
m/p-Xylene	634	83	13
o-Xylene	221	52	24
Ethylbenzene	288	32	11
1,3,5-Trimethylbenzene	297	65	22
ECD—			
1,1,1-Trichloroethane	190	26	14
Trichloroethene	121	30	25
Tetrachloroethene	108	19	17

The analytical procedure described here was also used to measure environmental (normal) VOC levels in human blood and has been found to be suitable. In Fig. 2 typical PID and ECD chromatograms of the blood sample of a female smoker smoking at least 20 cigarettes per day are shown indicating that the described procedure is appropriate for this application. The suitability of our procedure for biological monitoring of occupationally exposed persons has been proven by successful participation in an interlaboratory comparison program organized by the German Society for Occupational and Environmental Medicine (for results see Table 3).

Conclusion

The static headspace GC procedure described here offers a useful approach for the determination of toxicological relevant VOCs such as benzene, toluene, xylenes, ethylbenzene, trichloroethene and tetrachloroethene in blood. It is applicable for occupational as well as for environmental concentrations. The PID, a detector which is highly selective and sensitive for aromatic compounds and carbon–carbon double-bonds, was used in in-series combination with ECD and FID. The PID turned out to be by a factor of 14 to 32 more sensitive for the determination of aromatic hydrocarbons such as benzene, toluene, xylenes and ethylbenzene as the FID. Detection limits obtained with the system described here are comparable with those reported from other studies applying the dynamic headspace or purge and trap technique in combination with MS detection. Thus, an enrichment of these VOCs by dynamic headspace techniques is dispensable for the determination of ecological concentrations of these aromatic hydrocarbons in blood. The procedure described here is a viable alternative to the above mentioned procedures. Its main advantage is that it is simpler to use and needs a less costly and complex instrumentation. Compared with dynamic headspace techniques it is less

Table 7 Comparison of the results of the determination of benzene and toluene in spiked animal blood obtained with three different methods (the arithmetic means and standard deviations of 10 replicate measurements are given)

	Added/ ng l^{-1}	Static HS–PID/ ng l^{-1}	Dynamic HS–FID/ ng l^{-1}	Dynamic HS–ITD/ ng l^{-1}
Benzene	88	153 ± 27	114 ± 24	119 ± 24
Toluene	87	119 ± 19	70 ± 10	121 ± 20

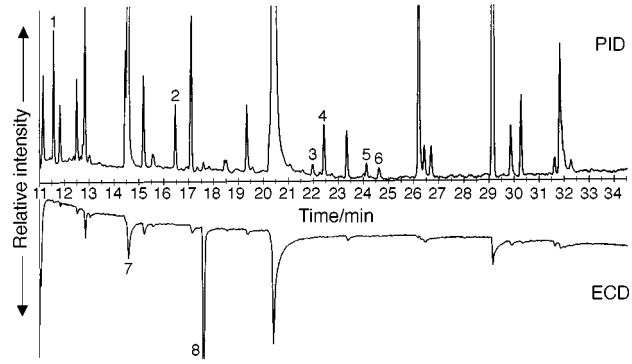

Fig. 2 PID and ECD chromatograms of the blood sample of a female smoker (1, benzene; 2, toluene; 3, ethylbenzene; 4, *m*-, *p*-xylene; 5, *o*-xylene; 6, styrene; 7, trichloroethene; 8, tetrachloroethene). The blood sample contained 250 ng l^{-1} benzene, 452 ng l^{-1} toluene, 1460 ng l^{-1} xylenes, < 4 ng l^{-1} trichloroethene and 420 ng l^{-1} tetrachloroethene.

prone to artifact formation and reduces the risk of sample contamination by impurities present in the purging gas.

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