ELSEVIER

Journal of Chromatography B, 714 (1998) 205–213

JOURNAL OF CHROMATOGRAPHY B

Headspace solid-phase microextraction and gas chromatographic determination of dinitroaniline herbicides in human blood, urine and environmental water

Fuyu Guan[1,a], Kanako Watanabe[a], Akira Ishii[a], Hiroshi Seno[a], Takeshi Kumazawa[b], Hideki Hattori[c], Osamu Suzuki[a,*]

[a] *Department of Legal Medicine, Hamamatsu University School of Medicine, 3600 Handa-cho, Hamamatsu 431-3192, Japan*
[b] *Department of Legal Medicine, Showa University School of Medicine, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142, Japan*
[c] *Department of Legal Medicine, Aichi Medical University, Nagakute-cho, Aichi 480-11, Japan*

Received 18 December 1997; received in revised form 5 May 1998; accepted 5 May 1998

Abstract

Solid-phase microextraction (SPME) is a unique extraction and sampling technique, and it has been used for separation of volatile organics from water or other simple matrices. In this study, we have used SPME to separate dinitroaniline herbicides from complicated matrices of human urine and blood in order to broaden its application to biomedical analysis. The SPME conditions were optimized for water, urine and blood samples, in terms of pH, salt additives, extraction temperature, and fiber exposure time. Urine or water (1.0 ml) spiked with herbicides and 0.28 g of anhydrous sodium sulfate was preheated at 70°C for 10 min, and a polydimethylsiloxane-coated fiber for SPME was exposed to the headspace at 70°C for another 30 min; while spiked blood (0.5 ml) diluted with water (0.5 ml) was treated at 90°C in the same way. The herbicides were extractable under these conditions, and could be determined by gas chromatography–electron capture detector (GC–ECD). The recoveries of the herbicides, measured at the concentrations of 0.50 and 1.0 ng/ml urine or water, or 6.0 and 20 ng/0.5 ml blood, ranged from 35 to 64% for different herbicides from water or urine, and from 3.2 to 7.2% from blood. The headspace SPME yielded clean extracts of dinitroaniline herbicides from urine, blood or water, which could be directly analyzed by GC–ECD without further purification. The peak areas of the extracted herbicides were proportional to their concentrations in the range 0.1–10 ng/ml in water or urine, or 1–60 ng/0.5 ml in blood. The lowest detectable concentration of the herbicides lay in 0.1 ng/ml water or urine, or in 0.5 ng/0.5 ml blood. The intra- and inter-day coefficients of variation were within 14% for most of the analytes. Although the recoveries of the herbicides were rather low, the linearity of calibration curve and the precision were good. The developed method is more sensitive and much simpler in sample preparation than previously reported ones. With the established SPME method, a dosed herbicide was successfully separated and determined in rats' blood.

Keywords: Dinitroaniline; Solid-phase microextraction

1. Introduction

Human blood and urine are quite common matrices for detection and identification of possible

*Corresponding author.
[1]On leave from Beijing Institute of Pharmacology and Toxicology, Beijing, People's Republic of China.

0378-4347/98/$19.00
PII: S0378-4347(98)00234-5

toxicants in both clinical toxicological examinations and forensic investigations. Traditionally, the toxicants, prior to identification and determination by analytical instruments, are separated from blood or urine by the conventional liquid–liquid extraction (LLE), which is sometimes a tedious and solvent-consuming process. In the 1980s, solid-phase extraction (SPE) was developed, and SPE cartridges and membranes have been employed to extract organic toxicants or drugs from these matrices. However, in both LLE and SPE, toxic organic solvents are used and multiple operational steps are needed. In 1990, a novel solvent-free solid-phase microextraction (SPME) technique was proposed by Pawliszyn and coworkers [1–4], which integrated sampling, extraction, concentration and sample introduction into a single step. This technique was found applicable to extraction of volatile organics including some herbicides from aqueous media [5–10] or from other simple matrices [11,12], before analysis by gas chromatography (GC). There are several reports, mainly from our laboratories, describing SPME of drugs or toxicants from blood and urine [13–27]. This article presents the experiments on headspace SPME separation of dinitroaniline herbicides from urine, blood and environmental water, to show the possibility of SPME from complicated sample matrices.

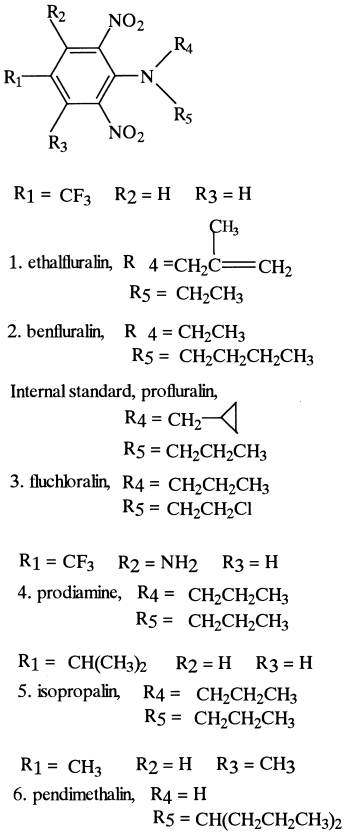

Fig. 1. Chemical structures of the herbicides used in this study.

2. Experimental

2.1. Reagents

The chemical structures of six dinitroaniline herbicides and an internal standard (I.S.) used in the present experiments are shown in Fig. 1. Ethalfluralin, fluchloralin, isopropalin, profluralin (I.S.) and benfluralin were purchased from Kanto (Tokyo, Japan); pendimethalin from GL Sciences (Tokyo, Japan); and prodiamine from Wako (Osaka, Japan). They were made into stock solutions of 1.0 mg/ml in methanol, and stored at 4°C. Working solutions were prepared by dilution of the stock solutions with methanol. Other chemicals used were of analytical grade. Blood and urine were obtained from healthy subjects. Water was taken during the winter season from a small river near Hamamatsu University.

2.2. GC conditions

A Shimadzu GC-14B gas chromatograph (Shimadzu, Kyoto, Japan), equipped with an electron capture detector (ECD) and a DB-1 capillary column (30 m×0.32 mm I.D., 0.25 μm of film thickness, J&W Scientific, Folsom, CA, USA), was used. The injector and detector temperatures were 270 and 300°C, respectively. Helium was used as carrier gas at a precolumn pressure of 80 kPa. The column temperatures were programmed as follows: 100°C (hold for 1 min) to 170°C (7 min), 190°C (3 min) and finally 300°C (5 min) at a constant rate of

20°C/min. Samples were injected in the splitless mode for 1 min, and then the splitter was opened. The ECD current was set at 1 nA, and the range at 10.

2.3. SPME procedures

The SPME device and its fibers were obtained from Supelco (Bellefonte, PA, USA). The fiber was 10-mm long, 100 μm in diameter, and coated with 100-μm thickness of polydimethylsiloxane. New fiber was conditioned for 1 h in a GC injection port at 250°C before samplings. The conditioned fibers were used immediately or protected from contamination by inserting the SPME syringe needle into a GC injection port septum before use.

A 1.0-ml aliquot of river water or urine was placed in a 4-ml glass vial with a silicone-septum cap (Supelco), spiked with I.S. and 0.1–10 ng of each herbicide, and mixed with 0.28 g (2 mmol) of anhydrous sodium sulfate. The vial was capped, and placed in a Reacti-Therm heater (Pierce, Rockford, IL, USA) at 70°C. After 10 min, the needle of the SPME device pierced the septum of the vial, and the fiber was exposed for 30 min to the headspace above the spiked urine or water which was kept at 70°C and stirred by a small PTFE-coated bar. Finally the fiber was retracted into the needle, pulled out from the vial and immediately inserted into the GC injection port at 270°C. It was exposed there for 5 min for complete desorption of analytes, although almost all of the herbicides were desorbed in the first minute.

The SPME of herbicides from human blood was conducted in the same way except that 0.5 ml of blood spiked with herbicides was mixed with 0.5 ml of distilled water, and was preheated at 90°C for 10 min and headspace-extracted at 90°C for 30 min; no salt was added to the mixture.

2.4. Animal experiments

Male Sprague–Dawley rats weighing about 200 g were anaesthetized by subcutaneous injection of 6.4 mg of sodium pentobarbiturate, and 0.5 h later they received an oral administration of 4 mg of benfluralin, which had been dissolved in 0.5 ml of cooking oil. Four hours after the administration, blood was taken from the abdominal aorta of the rats under anaesthesia, that was effected by another injection of sodium pentobarbiturate, mixed with heparin and NaF (each 2 mg/ml), and kept at 4°C until analysis. The control group of rats was treated in the same way except that no herbicide was administered. To 0.5 ml of the blood, 100 ng of profluralin (I.S.) and 2.5 ml of distilled water were added, and the blood was extracted in the same way as the human blood.

3. Results and discussion

3.1. Conditions for SPME of the herbicides

The important parameters influencing headspace SPME are fiber coatings, temperature, fiber exposure time, additives of inorganic salt, and occasionally pH, which decides the percentage of a free or ionic form of organic acids or bases and thus their partition between the headspace and solution. Fibers of polydimethylsiloxane and polyacrylate coatings

Table 1
Dilution effect on SPME efficiency for the analytes in blood[a]

Blood/water[b]	Ethalfluralin	Benfluralin	Fluchloralin	Prodiamine	Isopropalin	Pendimethalin	Profluralin
0.50 ml/0 ml	$2.74\cdot10^5$	$3.43\cdot10^5$	$1.40\cdot10^5$	$6.30\cdot10^4$	$1.31\cdot10^5$	$5.50\cdot10^4$	$2.23\cdot10^5$
0.50 ml/0.50 ml	$4.63\cdot10^5$	$5.75\cdot10^5$	$2.55\cdot10^5$	$1.48\cdot10^5$	$2.52\cdot10^5$	$1.24\cdot10^5$	$3.85\cdot10^5$
0.50 ml/1.0 ml	$4.61\cdot10^5$	$5.51\cdot10^5$	$2.09\cdot10^5$	$1.49\cdot10^5$	$2.03\cdot10^5$	$9.98\cdot10^4$	$3.26\cdot10^5$
0.50 ml/1.5 ml	$4.81\cdot10^5$	$5.75\cdot10^5$	$1.95\cdot10^5$	$5.83\cdot10^4$	$1.45\cdot10^5$	$5.81\cdot10^4$	$3.40\cdot10^5$

[a] Efficiency is expressed in terms of the peak area of extracted herbicides.
[b] Blood was spiked with 10 ng of each herbicide and the mixture was extracted at 70°C for 30 min.

were compared first; the former had higher extraction efficiency for dinitroaniline herbicides. Second, effects of salts and pH were examined. The herbicides were spiked to each aqueous solution containing the following uni- and divalent salts, and SPME efficiency was compared between these salts: NaCl (6 mol/l), NaH_2PO_4, NH_4Cl, KCl, $NaHCO_3$ (these four salts at 4 mol/l), $(NH_4)_2SO_4$, Na_2SO_4, $CaCl_2$, $K_2B_4O_7$, Na_2CO_3 (these five salts at 2 mol/l), NaOH (0.05 and 1 mol/l), and no salt added. When extracted from solutions of pH values from 4.7 (NaH_2PO_4 buffer) to 9.2 ($K_2B_4O_7$ buffer), the herbicides showed higher responses (recoveries) than those extracted from strongly basic solutions (from pH 12 to 14). This difference could not reasonably be explained by the weak-basic property of the dinitroaniline compounds. Among the salt additives tested, sodium sulfate was most effective in increasing the recoveries of the herbicides. Finally, the effect of temperature on SPME efficiency was examined and the results are presented in Fig. 2a. A suitable temperature for SPME of all six herbicides and the internal standard was 70°C for water and urine samples.

Blood tended to coagulate when it was treated in the same way as water or urine, and the recoveries of the herbicides were quite low. SPME conditions had to be reoptimized for blood samples. To solve this problem, we diluted blood with distilled water. Table 1 shows the dilution effect on SPME efficiency; when 0.5 ml of water was added to 0.5 ml of blood for dilution, the efficiency (peak area) was the highest for majority of the analytes. In addition, temperature dependence of headspace SPME of the analytes from blood was examined, as shown in Fig. 2b. A suitable temperature for SPME of the herbicides from blood was found at 90°C. From the viewpoint of SPME, blood is quite different to urine and water in that it is viscous and its compositional macromolecules like lipids and proteins may have an affinity to lipophilic organic compounds [13], preventing analytes' escape from blood samples into headspace phase. Thus, a higher temperature for headspace SPME was required for blood samples. The addition of sodium sulfate, which could enhance the extraction of the herbicides from water or urine, had a negative effect on the SPME efficiency of the analytes from blood. Thus, we did not add any salt to blood samples.

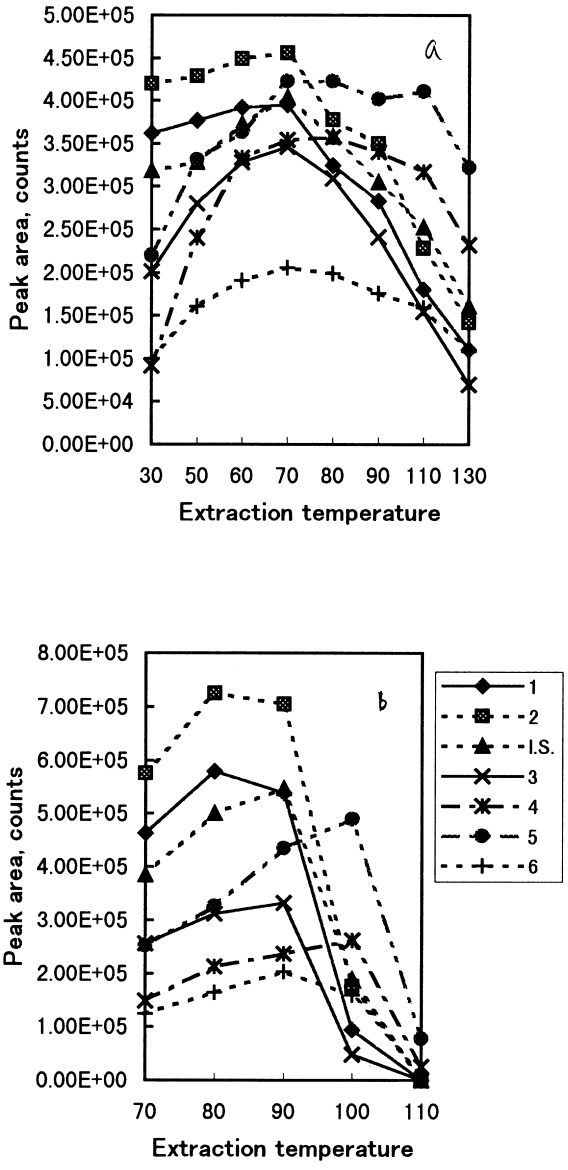

Fig. 2. Temperature profile of SPME of herbicides from water (a) or human blood (b). (a): 1.0 ml of H_2O spiked with 1.0 ng each of herbicides and 2 mmol of Na_2SO_4; or (b): 0.5 ml of blood plus 0.5 ml of H_2O spiked with 10 ng each of herbicides. Herbicide identities are: ethalfluralin (1), benfluralin (2), profluralin (I.S.), fluchloralin (3), prodiamine (4), isopropalin (5) and pendimethalin (6). Other conditions are indicated in Section 2.

The adsorption rates of the seven analytes includ-

ing the I.S. were tested as a function of headspace-exposure time for water, urine and blood samples (at 70°C for water or urine and at 90°C for blood). They rapidly increased up to 10 min and then increased gradually until 40 min. Thus, we adopted a 30-min exposure time.

The time profile of the desorption process of the herbicides adsorbed onto SPME fiber was observed in GC injection port at 270°C. All adsorbed herbicides and I.S. were almost completely desorbed within 1 min. Thus we set the splitless time of GC injector at 1 min.

On the basis of the above experiments, we chose the SPME conditions as follows: 1.0 ml of urine or water spiked with the herbicides, with addition of 2 mmol of anhydrous sodium sulfate, was extracted with polydimethylsiloxane coating fiber, at 70°C for 30 min. For whole blood, SPME was conducted in the same way except that 0.5 ml of blood was diluted with 0.5 ml of distilled water and headspace-extracted at 90°C for 30 min without any addition of salts.

3.2. Validation of the method

Urine, blood and water blanks, which were treated under the same SPME conditions chosen above, exhibited relatively clean chromatograms, as shown in Fig. 3; although there some impurities, they did not interfere with the peaks of the herbicides. In Fig.

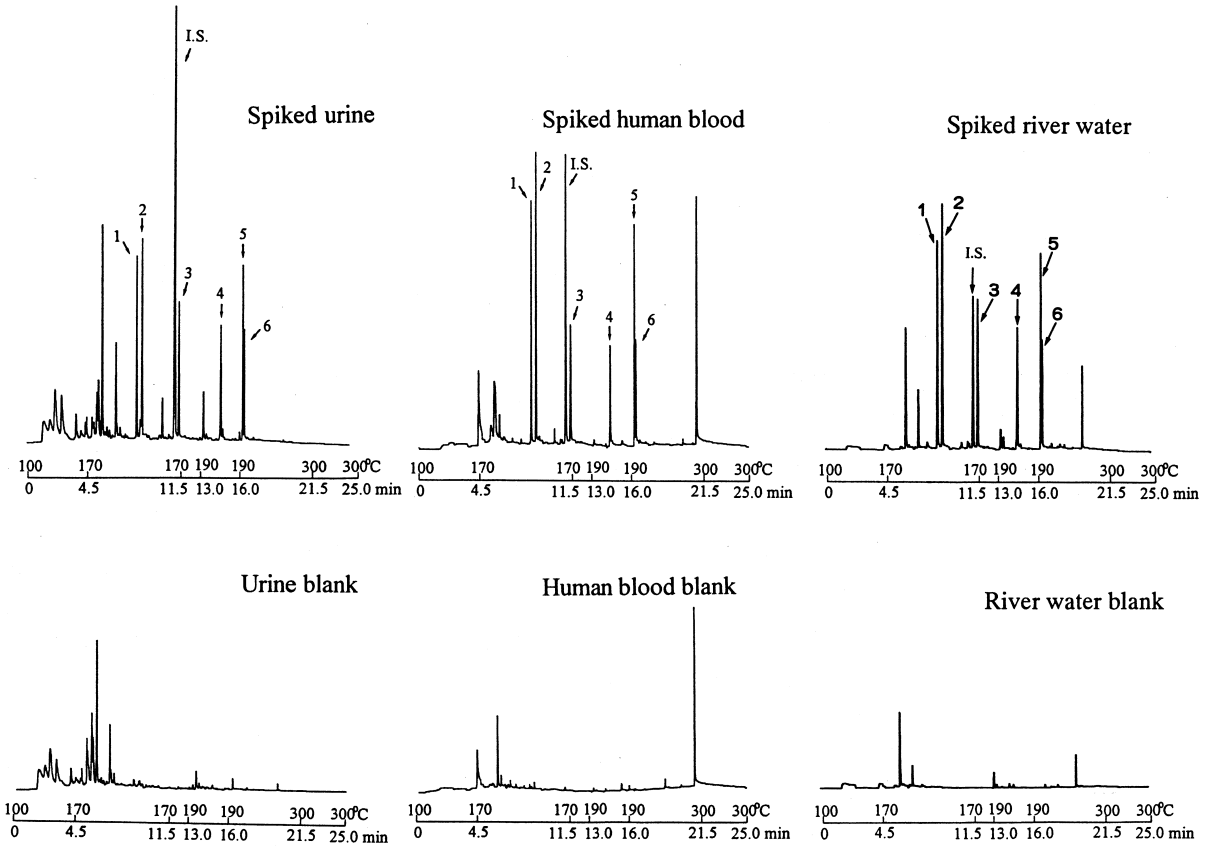

Fig. 3. GC–ECD chromatograms of the herbicides SPME-extracted from human urine, blood and river water. Urine (1.0 ml) spiked with 1.0 ng/ml of each herbicide and 10 ng/ml of I.S. was extracted at 70°C for 30 min, while human blood (0.50 ml, diluted with 0.50 ml of water) spiked with 6.0 ng of each herbicide and 10 ng of I.S. was extracted at 90°C for 30 min. River water (1.0 ml) spiked with 1.0 ng/ml of each herbicide and I.S. was extracted at 70°C for 30 min. Peak identities are the same as in Fig. 2.

Table 2
Percent SPME recoveries of dinitroaniline herbicides from human urine, blood and river water (mean±S.D., $n=6$)[a]

Compound	Recovery (%)					
	Urine		Blood		Water	
	0.5 ng/ml	1.0 ng/ml	6.0 ng/0.5 ml	20 ng/0.5 ml	0.5 ng/ml	1.0 ng/ml
Ethalfluralin	55±4.3	51±2.3	6.4±0.62	5.6±0.51	53±3.8	59±3.1
Benfluralin	54±4.2	53±2.1	7.2±0.71	6.2±0.52	–[b]	61±2.5
Fluchloralin	45±3.4	48±3.1	3.9±0.31	3.7±0.27	60±4.2	63±4.0
Prodiamine	17±3.9	40±1.8	3.4±0.30	3.2±0.17	50±4.1	54±2.9
Isopropalin	35±8.1	57±2.4	5.9±0.55	5.2±0.30	47±8.6	42±2.5
Pendimethalin	45±2.9	53±4.4	4.2±0.41	4.2±0.26	58±8.3	59±5.1
Profluralin	58±5.8	53±3.1	7.2±0.76	6.0±0.48	64±8.3	58±4.9

[a] Recoveries were measured by calibration of each external standard (5-point calibration for blood samples and duplicate two-point calibration for urine and water samples). Other conditions are indicated in Section 2.
[b] Not measured.

Table 3
Regression equations for the extracted herbicides against their concentration in urine, blood or river water[a]

Compound	$y=ax+b$[b]					
	a±S.D.[c]	b±S.D.[c]	r^2	a±S.D.[c]	b±S.D.[c]	r^2
Urine						
	(0.10, 0.20, 0.40, 0.60, 0.80, 1.0 ng/ml)			(1.0, 2.0, 4.0, 6.0, 8.0, 10 ng/ml)		
Ethalfluralin	1.08±0.05	0.059±0.030	0.992	0.10±0.005	0.14±0.03	0.988
Benfluralin	1.30±0.08	0.043±0.049	0.985	0.11±0.004	0.18±0.02	0.994
Fluchloralin	0.84±0.02	0.052±0.011	0.998	0.072±0.004	0.14±0.02	0.990
Prodiamine	0.74±0.05	0.051±0.020	0.990	0.066±0.004	0.13±0.03	0.984
Isopropalin	0.81±0.04	0.062±0.026	0.989	0.070±0.005	0.14±0.03	0.977
Pendimethalin	0.59±0.03	0.000±0.016	0.992	0.060±0.003	0.083±0.017	0.991
Blood						
	(1.0, 2.0, 4.0, 6.0, 8.0, 10 ng/0.5 ml)			(10, 20, 40, 60 ng/0.5 ml)		
Ethalfluralin	0.086±0.002	0.091±0.013	0.997	0.0091±0. 00057	0.13±0.022	0.992
Benfluralin	0.11±0.003	0.13±0.021	0.996	0.011±0.0008	0.16±0.029	0.989
Fluchloralin	0.054±0.001	0.075±0.008	0.998	0.0067±0.00029	0.080±0.011	0.996
Prodiamine	0.039±0.002	0.076±0.011	0.991	0.0063±0.00016	0.081±0.0059	0.999
Isopropalin	0.070±0.003	0.11±0.02	0.993	0.0082±0.00047	0.12±0.018	0.993
Pendimethalin	0.038±0.002	0.039±0.012	0.988	0.0054±0.00024	0.035±0.0091	0.996
River water						
	(0.10, 0.20, 0.40, 0.60, 0.80, 1.0 ng/ml)			(1.0, 2.0, 4.0, 6.0, 8.0, 10 ng/ml)		
Ethalfluralin	0.19±0.016	0.012±0.006	0.987	0.11±0.003	0.055±0.009	0.998
Benfluralin	0.27±0.018	0.015±0.007	0.991	0.14±0.002	0.095±0.008	0.999
Fluchloralin	0.21±0.009	0.011±0.004	0.996	0.090±0.004	0.089±0.012	0.995
Prodiamine	0.20±0.010	0.021±0.004	0.996	0.070±0.003	0.093±0.011	0.994
Isopropalin	0.27±0.004	0.008±0.002	0.999	0.10±0.003	0.12±0.009	0.998
Pendimethalin	0.16±0.006	0.002±0.002	0.997	0.081±0.002	0.061±0.007	0.998

[a] Concentration of I.S. (profluralin) was adjusted to match the different concentration range of herbicides: 1.0 or 10 ng/ml of I.S. was added to urine/water containing 0.1–1.0 or 1.0–10 ng/ml of herbicides, respectively; while 10 or 100 ng/ml of I.S. to blood containing 1.0–10 or 10–60 ng/ml of herbicides.
[b] y is the ratio of the peak area of analytes to that of I.S., and x is concentration of the herbicides in urine, blood or river water.
[c] Regression fitting was conducted by using Microsoft EXCEL software, and the slope and intercept values estimated by regression were expressed as mean value±standard deviation (X±S.D.) to show the uncertainty extent of these values.

3, the lower ECD response of prodiamine might be explained by the existence of Na primary amino group that decreases electron-capture power of the molecule.

The recoveries of the herbicides at two concentrations from urine, whole blood and water were measured with external calibration, as listed in Table 2. The purpose of using external standard calibration was to estimate the recoveries of all the herbicides including the I.S. The recoveries from water and urine ranged from 35 to 64% for different herbicides except for prodiamine at 0.5 ng/ml in urine, which showed only 17% recovery. The recoveries from whole blood ranged from 3.2 to 7.2%, which were much lower than those from water or urine.

The SPME-separated herbicides were quantified by I.S. calibration; profluralin was used as I.S. because of its stability and the fact that its peak was located in the middle of the analyte peaks. If it is present in a sample, one of other herbicides, which is absent in the sample, can be chosen as I.S.. The ratio of ECD responses (peak areas) SPME-separated herbicides to that of I.S. showed good linearity vs. concentration, as indicated in Table 3; the linear range was 0.1–10 ng/ml for urine or water samples, and 1.0–60 ng/0.5 ml for whole blood. The lowest detectable concentration was 0.1 ng/ml for all the analytes in urine or water, and 0.5 ng/0.5 ml in whole blood.

Intra- and inter-day precision and accuracy of the developed method was checked for urine, blood and water samples, as shown in Table 4. The intra- and inter-day precision expressed as coefficients of variation (C.V.s) were not more than 14% for all the herbicides except for prodiamine. The accuracy defined as deviation from spiked amounts was within ±20% for majority of the herbicides, in the intra- and inter-day measurements.

Although the SPME recoveries of the herbicides were rather low, the linearity of calibration curve and the precision of the present method are fairly good, and the detection limits for urine and blood samples are lower than those by solid-phase extraction [28–30].

Table 4
Intra-day and inter-day C.V.s of SPME of dinitroaniline herbicides in human urine, blood and river water ($n=6$)[a]

	Intra-day						Inter-day					
	Added (ng)	Found (ng)	C.V. (%)	Added (ng)	Found (ng)	C.V. (%)	Added (ng)	Found (ng)	C.V. (%)	Added (ng)	Found (ng)	C.V. (%)
Urine												
Ethalfluralin	0.5	0.52	5.1	1.0	1.1	6.7	0.5	0.41	7.3	1.0	1.1	10
Benfluralin	0.5	0.50	3.1	1.0	1.1	4.6	0.5	0.47	6.0	1.0	1.2	5.4
Fluchloralin	0.5	0.57	4.8	1.0	1.1	5.5	0.5	0.50	8.7	1.0	1.1	8.5
Prodiamine	0.5	0.48	3.6	1.0	1.0	14	0.5	0.29	24	1.0	0.50	28
Isopropalin	0.5	0.47	8.8	1.0	1.2	10	0.5	0.46	8.9	1.0	1.2	7.6
Pendimethalin	0.5	0.54	2.8	1.0	1.2	5.4	0.5	0.61	5.8	1.0	1.3	6.1
Blood												
Ethalfluralin	6.0	6.1	3.6	20	18	9.3	6.0	5.7	6.2	20	22	8.5
Benfluralin	6.0	5.9	3.8	20	18	8.0	6.0	6.4	6.1	20	23	8.7
Fluchloralin	6.0	6.6	3.3	20	18	3.7	6.0	6.2	4.3	20	22	8.4
Prodiamine	6.0	6.0	12	20	17	5.4	6.0	2.4	21	20	23	10
Isopropalin	6.0	6.4	7.7	20	18	7.7	6.0	5.5	6.2	20	23	5.5
Pendimethalin	6.0	6.4	0.84	20	19	3.5	6.0	7.2	8.6	20	22	5.0
River water												
Ethalfluralin	0.2	0.22	4.2	1.0	1.2	5.9	0.2	0.22	4.4	1.0	1.1	6.5
Benfluralin	0.2	0.23	12	1.0	1.2	8.2	0.2	0.25	14	1.0	0.60	11
Fluchloralin	0.2	0.19	6.3	1.0	1.1	7.3	0.2	0.23	9.4	1.0	1.0	10
Prodiamine	0.2	0.26	32	1.0	0.54	9.9	0.2	0.21	14	1.0	0.40	62
Isopropalin	0.2	0.20	9.0	1.0	1.0	9.0	0.2	0.23	7.8	1.0	0.80	5.8
Pendimethalin	0.2	0.19	12	1.0	1.0	7.7	0.2	0.26	8.8	1.0	1.1	7.9

[a] Inter-day C.V.s were measured on six separate days. The spiked herbicides were quantified by internal standard calibration.

3.3. Measurements of a dosed herbicide in rat blood

To further validate the SPME method developed above, we administered orally a representative herbicide (benfluralin) to four rats. Rat blood had to be diluted with more water (0.5-ml blood/2.5-ml water), as it was too viscous to be extracted. The dosed herbicide was separated and detected from the blood, as shown in Fig. 4. In the chromatogram, there are some peaks of unknown origin, but they did not overlap the peaks of the herbicides tested in this study.

The blood concentration of benfluralin 4 h after the administration was determined to be 5.3±1.3 ng (n=4) in 0.5 ml of blood. This experiment shows that the present method does work with real samples. No data on blood or urine concentrations of dinitroaniline herbicides in humans or animals after acute intoxication or chronic exposure are available in the literature to date.

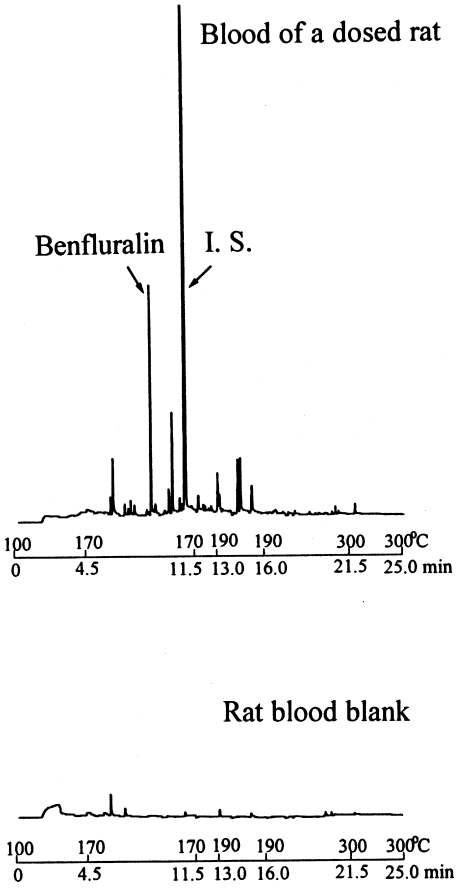

Fig. 4. GC–ECD chromatograms of dosed blood and its blank of rats extracted by SPME. The blood was taken 4 h after the administration of 4 mg of benfluralin. For other conditions, see Section 2.

4. Conclusion

We have been able to extract and detect dinitroaniline herbicides in urine, whole blood and environmental water by headspace SPME and capillary GC. From the viewpoint of simplicity, sensitivity, nonuse of organic solvents and easiness for automation, the present SPME method for dinitroaniline herbicides is recommendable for actual use in forensic, clinical and environmental toxicology.

Acknowledgements

Fuyu Guan is grateful to Ministry of Education, Science and Culture of Japan for its financial support with the fellowship.

References

[1] C.L. Arthur, J. Pawliszyn, Anal. Chem. 62 (1990) 2145.
[2] C.L. Arthur, L.M. Killam, K.D. Buchholz, J. Pawliszyn, J.R. Berg, Anal. Chem. 64 (1992) 1960.
[3] Z. Zhang, J. Pawliszyn, Anal. Chem. 65 (1993) 1843.
[4] Z. Zhang, M.J. Yang, J. Pawliszyn, Anal. Chem. 66 (1994) 844A.
[5] M.T. Sng, F.K. Lee, H.A. Lakso, J. Chromatogr. A 759 (1997) 225.
[6] J.J. Langenfeld, S.B. Hawthorne, D.J. Miller, Anal. Chem. 68 (1996) 144.
[7] K.J. Hageman, L. Mazeas, C.B. Grabanski, D.J. Miller, S.B. Hawthorne, Anal. Chem. 68 (1996) 3892.
[8] K. Jinno, T. Muramatsu, Y. Saito, Y. Kiso, S. Magdic, J. Pawliszyn, J. Chromatogr. A 754 (1996) 137.
[9] S. Magdic, J.B. Pawliszyn, J. Chromatogr. A 723 (1996) 111.
[10] A. Boyd-Boland, J. Pawliszyn, J. Chromatogr. A 704 (1995) 163.
[11] C. Grote, J. Pawliszyn, Anal. Chem. 69 (1997) 587.
[12] D.S. Forsyth, L. Dusseault, Food Addit. Contamin. 14 (1997) 301.
[13] S. Ulrich, J. Martens, J. Chromatogr. B 696 (1997) 217.

[14] W.E. Brewer, R.C. Galipo, S.L. Morgan, K.H. Habben, J. Anal. Toxicol. 21 (1997) 286.
[15] A. Namera, M. Yashiki, N. Nagasawa, Y. Iwasaki, T. Kojima, Forensic Sci. Int. 88 (1997) 125.
[16] X.P. Lee, T. Kumazawa, K. Sato, O. Suzuki, J. Chromatogr. Sci. 35 (1997) 302.
[17] F. Centini, A. Masti, I. Barni Comparini, Forensic Sci. Int. 83 (1996) 161.
[18] F. Degel, Clin. Biochem. 29 (1996) 529.
[19] N. Nagasawa, M. Yashiki, Y. Iwasaki, K. Hara, T. Kojima, Forensic Sci. Int. 78 (1996) 95.
[20] A. Ishii, H. Seno, T. Kumazawa, K. Watanabe, H. Hattori, O. Suzuki, Chromatographia 43 (1996) 331.
[21] H. Seno, T. Kumazawa, A. Ishii, M. Nishikawa, K. Watanabe, H. Hattori, O. Suzuki, Jpn. J. Forensic Toxicol. 14 (1996) 30.
[22] H. Seno, T. Kumazawa, A. Ishii, M. Nishikawa, K. Watanabe, H. Hattori, O. Suzuki, Jpn. J. Forensic Toxicol. 14 (1996) 199.
[23] A. Ishii, H. Seno, T. Kumazawa, M. Nishikawa, K. Watanabe, H. Hattori, O. Suzuki, Jpn. J. Forensic Toxicol. 14 (1996) 228.
[24] T. Kumazawa, K. Sato, H. Seno, A. Ishii, O. Suzuki, Chromatographia 43 (1996) 59.
[25] X.P. Lee, T. Kumazawa, K. Sato, Int. J. Legal Med. 107 (1995) 310.
[26] X.P. Lee, T. Kumazawa, K. Sato, O. Suzuki, Chromatographia 42 (1995) 135.
[27] M. Krogh, K. Johansen, F. Tonnesen, K.E. Rasmussen, J. Chromatogr. B 673 (1995) 299.
[28] T. Kumazawa, K. Sato, H. Seno, A. Ishii, O. Suzuki, J. Anal. Toxicol. 19 (1995) 95.
[29] S.D. West, H.H. Weston, E.W. Day Jr., J. Assoc. Off. Anal. Chem. 71 (1988) 1082.
[30] P. Cabras, M. Melis, L. Spanedda, C. Tuberoso, J. Chromatogr. 585 (1991) 164.