Available online at www.sciencedirect.com

ScienceDirect

Forensic Science International 175 (2008) 85–92

Forensic Science International

www.elsevier.com/locate/forsciint

Comparison and classification of methamphetamine seized in Japan and Thailand using gas chromatography with liquid–liquid extraction and solid-phase microextraction

Kenji Kuwayama [a,b,*], Hiroyuki Inoue [a], Juthamard Phorachata [c], Kanyanan Kongpatnitiroj [c], Vichet Puthaviriyakorn [c], Kenji Tsujikawa [a], Hajime Miyaguchi [a], Tatsuyuki Kanamori [a], Yuko T. Iwata [a], Naoki Kamo [b], Tohru Kishi [a]

[a] *National Research Institute of Police Science, 6-3-1, Kashiwanoha, Kashiwa, Chiba 277-0882, Japan*
[b] *Laboratory of Biophysical Chemistry, Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan*
[c] *Office of the Narcotics Control Board, Scientific Narcotics Detection Division, 5 Din-Deang, Bangkok 10400, Thailand*

Received 22 March 2007; received in revised form 2 May 2007; accepted 12 May 2007
Available online 13 June 2007

Abstract

Methamphetamine (MA) is one of the most frequently abused drugs worldwide. The aim of this study is to improve the analytical method for profiling MA impurity in order to compare and classify MA crystals seized in different countries and to investigate the relationships between seizures. To compare MA samples seized in Japan and Thailand, the following analytical method was adopted. A 50 mg sample of MA·HCl was dissolved in 1 ml of buffer solution (four parts 0.1 M phosphate buffer, pH 7.0, and one part 10% Na_2CO_3), impurities were extracted with 0.5 ml of ethyl acetate containing four internal standards (*n*-decane, *n*-pentadecane, *n*-eicosane and *n*-octacosane) and analyzed by gas chromatography with a flame ionization detector on a DB-5 capillary column (0.32 mm i.d. × 30 m, film thickness 1.0 μm). Fourteen characteristic peaks on chromatograms were selected for the comparison and classification of samples, and the data were evaluated by the Euclidean distance of the relative peak areas after logarithmic transformation. Sixty-nine samples seized in Japan and 42 seized in Thailand were analyzed. The samples were classified into four groups roughly by cluster analysis. In addition, when it was difficult to compare samples that had fewer impurities on chromatograms obtained from liquid–liquid extraction (LLE), solid-phase microextraction (SPME) was effective. Because many characteristic peaks were detected using SPME, SPME made it easy to compare samples of high purity. The combination of LLE and SPME was useful for impurity profiling of MA samples seized in different countries.

Keywords: Methamphetamine; Impurity profiling; GC; Japan; Thailand; SPME

1. Introduction

Methamphetamine (MA) is currently the major drug of abuse in Japan [1]. There, more than 80% of all reported violations of drug control laws involved MA. In 1999, a total of about 2000 kg was seized. The majority of the illicit MA circulated in Japan is smuggled from abroad [1]. Illicit MA in Japan is generally circulated in the form of white crystals, called "ice", at purity levels that have grown very high (generally in excess of 95%). On the other hand, the major illicit drug in Thailand is MA in tablets that also contain caffeine and other substances (starch, pigments and flavor compounds), called "Ya-Ba". Recently in Thailand, the seizure of MA tablets has been decreasing year after year, while that of MA crystals has been increasing sharply. As in Japan, in Thailand purity has become very high.

Therefore, international cooperation in criminal investigations is necessary to combat the spread of MA. Classification of seized MA by impurity profiling can provide very useful information in criminal investigations aimed at identifying drug traffic routes, the sources of supply and relationships between seizures [2]. A number of methods have been reported for MA impurity profiling, including the use of gas chromatography

---

* Corresponding author at: National Research Institute of Police Science, 6-3-1, Kashiwanoha, Kashiwa, Chiba 277-0882, Japan. Tel.: +81 4 7135 8001; fax: +81 4 7133 9173.
E-mail address: kuwayama@nrips.go.jp (K. Kuwayama).

0379-0738/$ – see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.forsciint.2007.05.013

(GC) [3–7], GC–mass spectrometry (MS) [8,9], high-performance liquid chromatography and capillary electrochromatography [10] and capillary electrophoresis (CE) [11]. The analytical methods for impurity profiling of MA tablets are similar to those of MA crystal [12]. Recently, we reported methods to analyze impurities in MA using GC–MS coupled with solid-phase microextraction (SPME) [13] and thermal desorption (TD) [14] instead of liquid–liquid extraction (LLE). Because the methods using SPME and TD enabled the extraction of volatile compounds in simple, rapid and solvent-free fashion, these approaches were useful and effective for MA impurity profiling, and they also provided supplementary information relative to results obtained by the LLE method.

In order to share profiling data between laboratories (in national and international databases) for chemical links between samples, it would be desirable to analyze MA seizures using the same method, to permit the evaluation of profiles by visual and/or computer-aided comparisons. From this point of view, capillary GC with a flame ionization detector (FID) would be suitable because of its good reproducibility, compared to other analytical tools such as CE and MS [11,13,14].

Two GC methods for impurity profiling are shown in Table 1. One is the method for MA impurity profiling adopted in our laboratory, that of the National Research Institute of Police Science (NRIPS) as well as by the Japanese Police (NRIPS method). The other is for impurity profiling of MA tablets adopted by the Office of the Narcotics Control Board (ONCB), Thailand (ONCB method). These methods have much in common in terms of extraction of impurities by ethyl acetate under basic conditions, although there are minor differences in sample amounts, the internal standard (IS) used and GC conditions such as column size and injector temperature. The aim of the study is to improve the analytical method for impurity profiling of MA crystals by GC with an FID, in order to compare and classify samples seized in different countries and to investigate the relationship between seizures.

2. Materials and methods

2.1. Reagents and chemicals

MA·HCl crystals seized in Japan and Thailand in recent years were used. MA samples in Thailand were obtained from ONCB. Authentic standards of *d*-MA·HCl (Philopon) and *l*-ephedrine·HCl were purchased from Dainippon Pharmaceutical Co. (Osaka, Japan). *dl*-Dimethylamphetamine·HCl and *cis*-1,2-dimethyl-3-phenylaziridine were synthesized in our laboratory, as previously reported [3,15–19]. *n*-Alkanes for ISs were purchased from Tokyo Kasei Kogyo Co. (Tokyo, Japan). All other solvents and reagents were of analytical grade and were purchased from Wako Pure Chemical Industries (Osaka, Japan). An SPME holder and fiber coated with divinylbenzene/carboxen/polydimethylsiloxane (DVB/CAR/PDMS) and an inlet liner for SPME were purchased from Supelco (Bellefonte, PA, USA).

2.2. LLE procedure

A 50 mg sample of MA·HCl was dissolved in 1 ml of buffer solution (four parts 0.1 M phosphate buffer, pH 7.0, and one part 10% (w/v) Na_2CO_3). The solution was extracted with 0.5 ml of ethyl acetate containing four ISs (*n*-decane (C_{10}, IS1), *n*-pentadecane (C_{15}, IS2), *n*-eicosane (C_{20}, IS3) and *n*-octacosane (C_{28}, IS4), each at a concentration of 0.02 mg/ml). After centrifuging the solution for 5 min at 3000 rpm, the organic layer was transferred into an insert of a GC microvial for automatic sampling.

2.3. SPME procedure

A 10 mg sample of MA·HCl was placed in a GC microvial, which was then sealed with a septum attached to a screw cap. Sampling was done in a chemical-free room to minimize atmospheric background contamination. To eliminate carry-over, an SPME fiber was conditioned with a GC inlet at 240 °C for over 30 min just prior to use. The fiber was inserted into the vial and exposed to the headspace inside the vial at 85 °C for 35 min. After the extraction, the fiber was immediately inserted into a GC inlet, and the compounds were desorbed and analyzed by GC.

2.4. Gas chromatographic analysis

Gas chromatographic analyses were carried out on an Agilent (Santa Clara, CA, USA) 6890 gas chromatograph equipped with an FID and an Agilent 7683 automatic sampler. The column was a DB-5 capillary column (0.32 mm

Table 1
Analytical procedures used for impurity profiling of MA crystals by the NRIPS method and for impurity profiling of MA tablets by the ONCB method

	NRIPS method	ONCB method
Sample	0.05 g	0.1 g
Reagents	0.1 M Phosphate buffer, pH 7 −10% Na_2CO_3, (4:1), 1 ml	0.1 M Phosphate buffer, pH 7, 1 ml 10% Na_2CO_3, 0.25 ml
Solvent	Ethyl acetate, 0.5 ml	Ethyl acetate, 0.4 ml
Internal standards	*n*-Decane (C_{10}) *n*-Pentadecane (C_{15}) *n*-Eicosane (C_{20}) *n*-Octacosane (C_{28})	*n*-Triacontane (C_{30})[a]
Column	DB-5 (Agilent), 0.32 mm i.d. × 30 m × 1.0 μm	Ultra-2 (Agilent), 0.2 mm i.d. × 25 m × 0.33 μm
Oven temperature	50 °C (1 min), 10 °C/min to 300 °C (10 min)	50 °C (1 min), 10 °C/min to 300 °C (15 min)
Injection temperature	240 °C	280 °C
Detection temperature	300 °C	280 °C
Carrier gas	He, 2 ml/min (constant flow)	He (constant pressure[b])
Injection volume	1 μl, splitless (1 min)	1 μl, splitless (1.2 min)

[a] The ethyl acetate solution containing *n*-tetradecane (C_{14}), C_{20} and C_{30} was analyzed as the external standards for retention time correction before sample analysis.

[b] The pressure was adjusted so that the retention time of C_{30} was in the range of 26.0–27.0 min.

Table 2
Peaks selected for data processing in the NRIPS method

Peak no.	Compound	Retention time (min)
1	IS1 (C_{10})	9.500
2	*cis*-1,2-Dimethyl-3-phenylaziridine[a]	11.600
3	Dimethylamphetamine[a]	13.620
4	Ephedrine[a] (pseudoephedrine)[b]	15.370
5	IS2 (C_{15})	16.700
6	Unknown	19.460
7	Unknown	20.040
8	IS3 (C_{20})	22.100
9	Unknown	23.070
10	1,3-Dimethyl-2-phenylnaphthalene[c]	23.188
11	1-Benzyl-3-methylnaphthalene[c]	23.396
12	MA dimer[c]	24.130
13	Unknown	24.290
14	Unknown	24.440
15	Unknown	24.610
16	Unknown	25.060
17	Unknown	25.600
18	IS4 (C_{28})	29.700

[a] Peaks identified by both retention times and mass spectra compared with those of authentic standards.

[b] Ephedrine and pseudoephedrine were not separated by the NRIPS method.

[c] Peaks presumed from mass spectra as reported previously.

i.d. × 30 m, film thickness 1.0 μm). The oven temperature was programmed as follows: 50 °C for 1 min, 10 °C/min to 300 °C, and then hold at 300 °C for 10 min. The injector and detector temperatures were set at 240 and 300 °C, respectively. Helium was used as the carrier gas at a constant column flow rate of 2 ml/min. Injection of 1 μl of the extract was made in the splitless mode (purge on time; 1.0 min). Agilent Chemstation software was used to control the GC system, data acquisition and integration of the gas chromatograms. Data were acquired at a rate of 20 Hz and a peak width of 0.05 min.

The GC analytical conditions for SPME were the same as those for LLE except for the inlet liner (0.75 mm i.d. for SPME) and the hold time at 300 °C (2 min). GC–MS analysis of the major impurity peaks was performed on an Agilent 6890 gas chromatograph with an Agilent 5973N MSD. The GC conditions were the same as mentioned above.

2.5. Data processing for LLE

Peak data integrated by the Chemstation software were further processed using the Drug Micro-Component Analysis & Comparison System (DMCPS) (Entest Japan, Tokyo, Japan). The peak retention times were corrected with those of four ISs that emerged immediately before and after the peaks. The peaks selected and their retention times are shown in Table 2. Each peak area was calculated relative to IS4, and common logarithms of 1000 times their relative areas were used for the calculation of Euclidean distances between any two chromatograms. In cases where the peak areas relative to IS4 were between 0 and 0.01, a value of 0.01 was assigned. Hierarchical cluster analysis using the Ward method was used to visualize the classification of samples.

2.6. Data processing for SPME

Peak data integrated by the Chemstation software were further processed using DMCPS and Microsoft Excel. Peaks derived from a fiber and a GC microvial emerged in the chromatogram obtained from an empty vial without ISs such as *n*-alkanes were used for correction of the retention times. The peaks selected and their retention times are shown in Table 3. Common logarithms of 1000 times the absolute area of each peak were used for the calculation of Euclidean distances between any two chromatograms. Hierarchical cluster

Table 3
Peaks selected for data processing of SPME method

Selected peak	Retention time (min)	Number of occurrences[a]	Major *m*/*z*	Tentative or confirmed compound
	2.85	15	43, 61, 70	Ethyl acetate
	3.08	2	91, 61, 40	
	3.33	1	77, 45	
	4.20	2	91, 43	
1	8.87	11	106, 105, 77	Benzaldehyde
	8.96	14	281	Octamethylcyclotretrasiloxane
	9.06	15	57, 43, 70	
	9.12	15	59, 43, 70	
2	11.64	15	91, 43, 134	Benzyl methyl ketone
	11.70	10	92, 45	1-Phenyl-2-propanol
IS1	11.73	15[b]	355, 267, 73	Decamethylcyclopentasiloxane
3	12.12	13	105, 122, 77	Benzoic acid
4	12.22	12	105, 77, 43	1-Phenyl-1,2-propanedione
	12.60	15	58, 91	MA
	13.25	15[b]	71, 89, 56	
	13.41	15[b]	113, 55, 85	
5	13.57	15	72	Dimethylamphetamine
IS2	14.28	15[b]	341, 73, 325	
	16.37	15[b]	71, 43, 83	
IS3	16.58	15[b]	281, 147, 73	
6	16.93	15	86, 58, 118	*N*-Formyl MA
	17.83	15[b]	149, 177	Diethyl phthalate
7	18.21	11	58, 100, 91	*N*-Acetyl MA
IS4	18.62	15[b]	355, 281, 221	
	19.52	14	147, 73	
	20.09	15	43, 86	
	20.38	12[b]	73, 147, 355	
	21.04	15[b]	149	Dibutyl phthalate

[a] Peaks with absolute areas over 100 were defined as occurrences.

[b] Also detected from a blank.

analysis using the Ward method was used to visualize the classification of samples.

3. Results and discussion

3.1. Optimization of analytical procedure

The analytical procedures for impurity profiling of MA crystal were examined. A sample of an MA crystal was analyzed by the ONCB method, which was optimized for the analysis of MA tablets. Because an MA tablet usually consists of MA·HCl (20–30%), caffeine (60–70%) and other substances, the gas chromatogram obtained from an MA tablet has many kinds of impurities at high levels. Fig. 1A shows a typical chromatogram obtained from an MA tablet. Besides huge MA and caffeine peaks, relatively large impurity peaks were detected. On the other hand, most MA crystals have high purity (more than 95%). The chromatogram obtained from MA crystal had few impurities at low levels (Fig. 1B). Because it was difficult to compare these low-impurity chromatograms obtained from the ONCB method, it was necessary to optimize the analytical procedures for impurity profiling of MA crystals.

The NRIPS method was developed for profiling high-purity MA seized in Japan, as reported previously [20], and minor modifications were done for the present study. The injector temperature was changed from 250 to 240 °C to restrain the decomposition of impurities by heat, and IS3 (C_{19}) and IS4 (C_{26}) were changed to C_{20} and C_{28}, respectively, for separating the impurities from each other. The NRIPS and ONCB methods have much in common with each other in terms of extraction of impurities by ethyl acetate under basic conditions. They, however, differ in sample amounts for extraction, IS used and GC conditions such as column size and injector temperature. Fig. 1C shows the chromatogram obtained from the same MA crystal using the NRIPS method. The differences in analytical procedures slightly affected the detection and separation of minute impurities. Various MA crystals were analyzed using the NRIPS method (Fig. 2). Some characteristic peaks were detected. The peaks of *cis*-1,2-dimethyl-3-phenylaziridine (Peak 2: 11.60 min), dimethylamphetamine (Peak 3: 13.62 min) and ephedrine (pseudoephedrine) (Peak 4: 15.37 min) were identified by both retention times and mass spectra compared with those of authentic standards. Ephedrine and pseudoephedrine were not separated by the NRIPS method. Three peaks (Peak 10: 23.19 min, Peak 11: 23.40 min and Peak 12: 24.13 min) were presumed to be 1,3-dimethyl-2-phenylnaphthalene, 1-benzyl-3-methylnaphthalene and MA dimer, respectively, in agreement with mass spectra as reported previously [18,21,22].

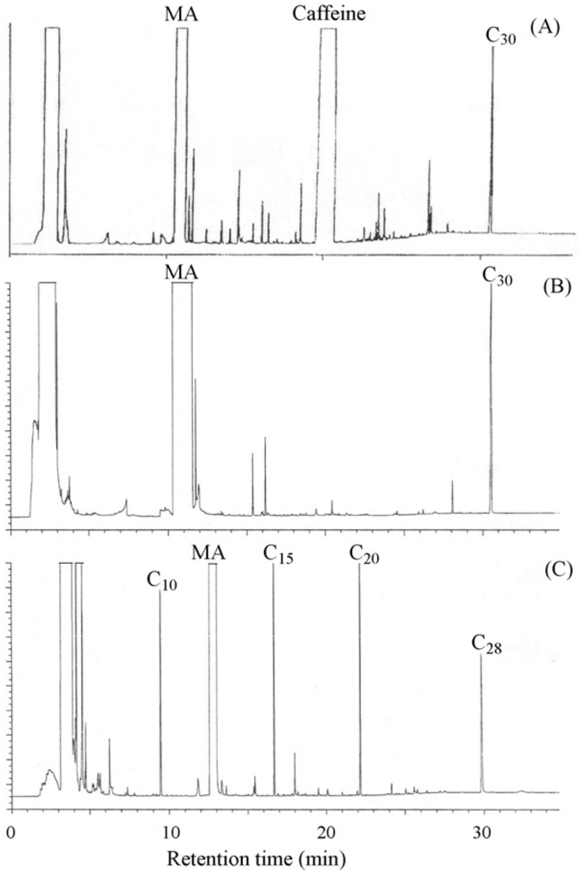

Fig. 1. Chromatograms obtained from an MA tablet and an MA crystal using the ONCB method and the NRIPS method. An MA tablet (A) was analyzed using the ONCB method. The same MA crystal was analyzed using the ONCB method (B) and the NRIPS method (C). Extraction and chromatographic conditions were shown in Table 1.

The chromatograms obtained from the same MA crystal with the ONCB and NRIPS methods were compared (Fig. 1B and C). A broadening of the MA peak was occasionally observed in the ONCB method, where a 0.2 mm i.d. capillary column was used (Fig. 1B). Minute impurity peaks were

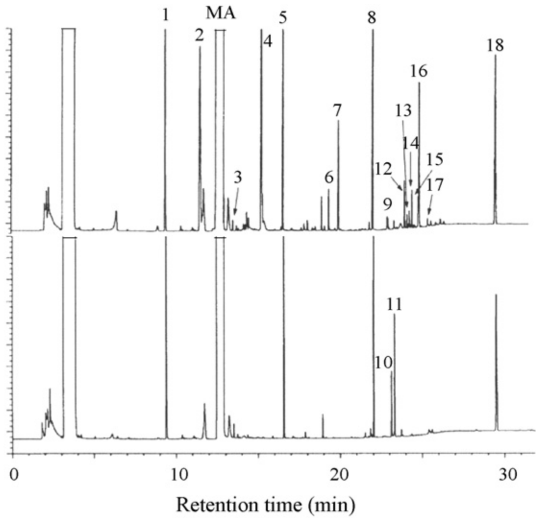

Fig. 2. Typical chromatograms obtained from MA crystals using the NRIPS method. MA crystals were analyzed using the NRIPS method as shown in Table 1. Peaks 1–18 were selected for data processing as shown in Table 2. Peaks 1, 5, 8 and 18 represent the IS peaks (C_{10}, C_{15}, C_{20} and C_{28}, respectively) used for the retention time correction. Peaks 2, 3 and 4 were identified as *cis*-1,2-dimethyl-3-phenylaziridine, dimethylamphetamine and ephedrine (pseudoephedrine), respectively, by both retention times and mass spectra compared with those of authentic standards. Peaks 10, 11 and 12 were presumed to be 1,3-dimethyl-2-phenylnaphthalene, 1-benzyl-3-methylnaphthalene and MA dimer, respectively, from mass spectra as reported previously.

detected in the case of the NRIPS method using a 0.32 mm i.d. capillary column (Fig. 1C), which was developed for profiling high-purity MA seized in Japan. It should be noted that the NRIPS method separated *cis*-1,2-dimethyl-3-phenylaziridine (11.60 min, Peak 2 in Fig. 2) and amphetamine (11.77 min) peaks that appeared before an MA peak, while the two compounds emerged together or as an incomplete peak in the ONCB method. In addition, the precision of retention time correction for data processing could be improved by increasing the number of IS (C_{10}, C_{15}, C_{20} and C_{28}) in the NRIPS method, while only one IS (C_{30}) for sample analysis was used in the ONCB method after the ethyl acetate solution containing *n*-tetradecane (C_{14}), C_{20} and C_{30} was analyzed as the external standards. C_{10}, C_{15}, C_{20} and C_{28} were carefully selected for ISs from a series of hydrocarbons, to obtain peaks that did not overlap with those from possible impurity peaks. Therefore, the NRIPS method was considered more efficient than the ONCB method for the comparison and classification of MA crystals.

3.2. Cluster analysis of samples seized in Japan and Thailand

MA crystals seized in Japan (69 samples) and Thailand (42 samples) were analyzed by the NRIPS method. Fourteen characteristic impurity peaks were selected for the following data processing (Fig. 2 and Table 2). Selected peaks included unknown peaks. Although it was impossible to identify the unknown peaks by GC–MS, the selected unknown peaks used for data processing were evaluated fully as reported previously [20]. Fig. 3 shows the dendrogram obtained from samples seized in Japan and Thailand. Samples tested were classified roughly into four groups (A–D). Fig. 4 shows the typical chromatograms of MA samples in each group (A–D) using the NRIPS method. Samples in group A were of high purity, containing low levels of few impurities (Fig. 4A). Fifteen samples were seizures in Japan, out of 34 samples in group A. Some of samples in group B (25 samples) were characterized by naphthalene derivatives such as 1,3-dimethyl-2-phenylnaphthalene and 1-benzyl-3-methylnaphthalene (peaks 1 and 2 in Fig. 4B) and group B had no sample seized in Thailand. High

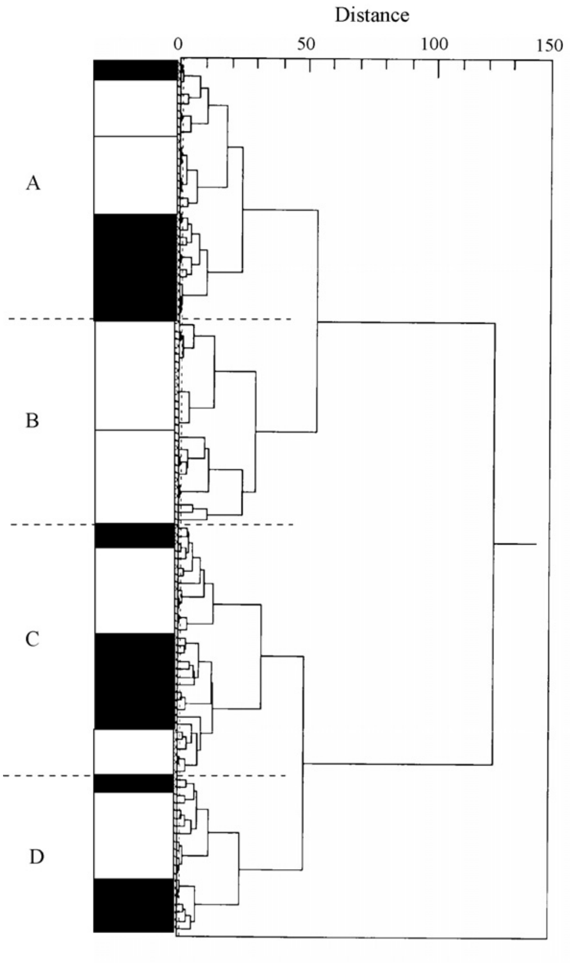

Fig. 3. Dendrogram obtained from a cluster analysis of MA crystals seized in Japan and Thailand. Sixty-nine samples seized in Japan and 42 samples in Thailand were classified into four groups (A–D). Open and solid bars represent clusters formed by samples in Japan and Thailand, respectively. The numbers of samples (Japan/Thailand) classified into each group are 15/19 for A, 25/0 for B, 17/15 for C and 12/8 for D.

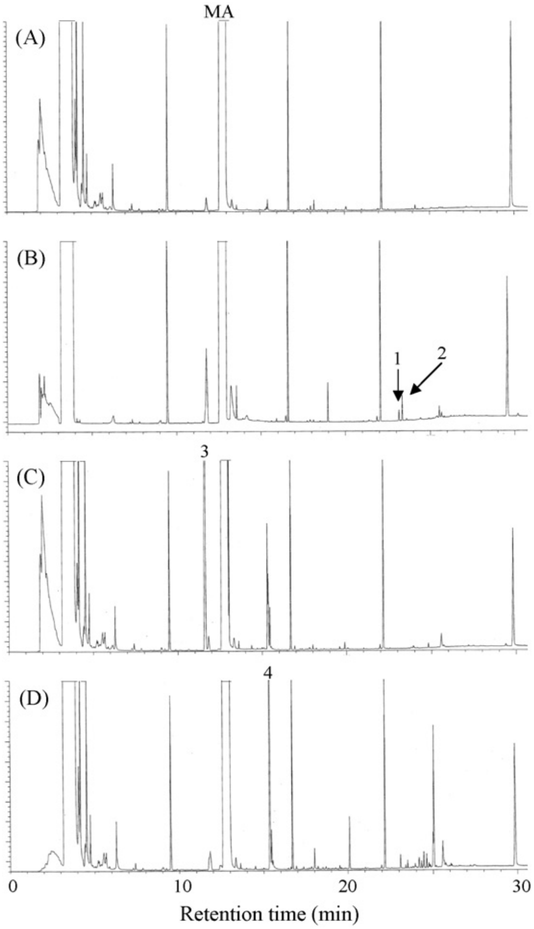

Fig. 4. Typical chromatograms of MA samples in each group using the NRIPS method. Samples in groups A–D were analyzed using the NRIPS method as shown in Table 1. Peak 1, 1,3-dimethyl-2-phenylnaphthalene; Peak 2, 1-benzyl-3-methylnaphthalene; Peak 3, *cis*-1,2-dimethyl-3-phenylaziridine; Peak 4, ephedrine (pseudoephedrine).

levels of *cis*-1,2-dimethyl-3-phenylaziridine (Peak 3 in Fig. 4C) and high levels of ephedrine (pseudoephedrine) (Peak 4 in Fig. 4D) were detected from some samples in groups C (32 samples) and D (20 samples), respectively. Group C and D had 17 and 12 samples seized in Japan, respectively. This method enabled the classification of samples by characteristic peaks such as naphthalene derivatives, *cis*-1,2-dimethyl-3-phenylaziridine and ephedrine (pseudoephedrine), and the dendrogram indicated the characteristics and tendencies of samples in different countries. The samples in the high-purity group (group A in Fig. 3) accounted for approximately one-fourth of the whole. Because it was difficult to compare chromatograms of samples in the high-purity group, an analytical method applicable to the comparison and classification of such samples in detail was necessary.

3.3. Comparison and classification of samples in the high-purity group by SPME

Because the chromatograms obtained from MA samples in the high-purity group have few impurities, it is impossible to visually compare samples in the high-purity group. SPME is simply and rapidly prepared, effective for volatile compounds and nondestructive to the sample. The approach we reported previously [13] was useful and effective for the impurity profiling of MA, and it provided supplementary information relative to the results of a conventional analysis using LLE. Samples in the high-purity group were examined using SPME. Although our method [13] was used for the extracting condition, GC instead of GC–MS was used for the analysis because it was economical and convenient to use the same GC instrument and GC conditions as in the case of LLE. First, an SPME fiber was inserted into an empty vial without neither MA nor *n*-alkanes, and then extracted and analyzed by GC (Fig. 5A). The chromatogram had some large peaks, which GC–MS analysis confirmed were compounds containing siloxanes. They were considered to derive from the coating of an SPME fiber or a GC microvial. When *n*-alkanes as ISs were put into a vial and analyzed by SPME method, some impurities in *n*-alkanes as well as *n*-alkanes themselves were also detected. They were not detected in the case of LLE. Because the peaks were also detected from the same type and different lots of fibers with different intensities, the peaks (ISs 1–4 in Fig. 5A and Table 3) derived from an empty vial were used for not peak area correction but retention time correction.

When MA crystals were extracted with SPME and analyzed by GC (SPME method), the chromatograms had many impurities (Fig. 5B–D) while the chromatograms in the case of LLE had few impurities. In the SPME method, it was easy to compare the samples visually from the chromatograms as shown in Fig. 5B–D. Fifteen samples in the high-purity group, which belong to group A in Fig. 3, were analyzed by the SPME method. In addition, SPME-GC–MS analysis was performed in the same GC conditions as for LLE in order to seek characteristic peaks for data processing (Table 3). Seven characteristic peaks, which were identified or estimated from mass spectra, were selected for comparison and classification of samples. Cluster analysis of samples in the high-purity group was performed using these seven peaks (Fig. 6). Samples shown in Fig. 5B were distinguished clearly from those in Fig. 5C and D using the SPME method, whereas in the case of LLE it was difficult to compare and classify samples in the high-purity group because there were so few impurities. The SPME method enabled us to compare and classify high-purity MAs in detail.

3.4. MA impurity profiling for the future

Because the abuse of MA is a worldwide social problem, the international cooperation of criminal investigation is important to prevent the spread of this drug. To the best of our knowledge, this is the first report to compare and classify MA seized in different countries. Although MA impurity profiling has been reported in many individual countries, such as Korea [22], Australia [23] and the Philippines [24], and a harmonized method for the profiling of amphetamines in European

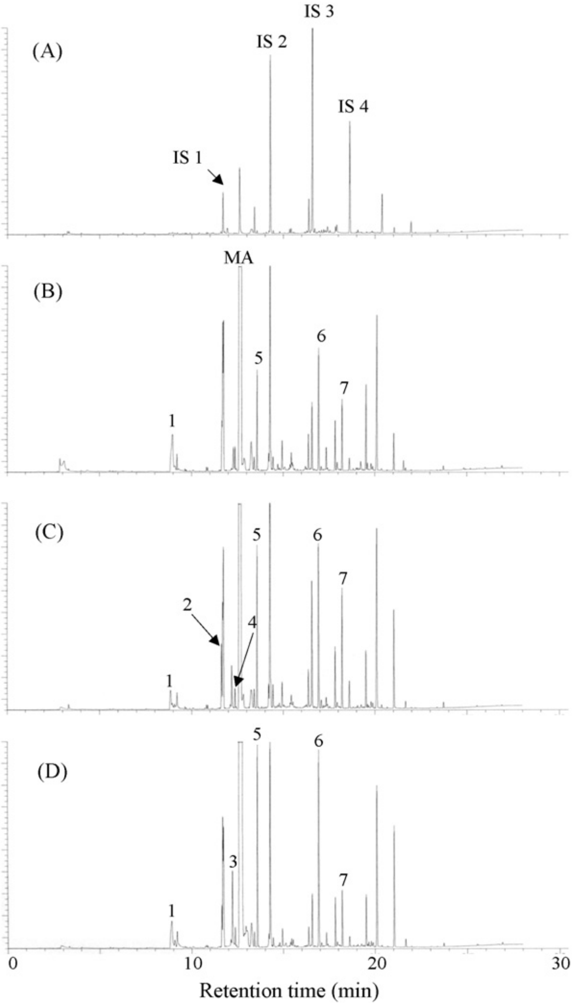

Fig. 5. Typical chromatograms obtained from a blank and samples by the SPME method. (A) An empty vial without MA was used. (B)–(D) A different MA sample (10 mg) in the high-purity group was put into each vial. Each vial was sealed with a screw cap. The SPME fiber was inserted into the vial and exposed to the headspace as described elsewhere. Peaks 1–7 were selected for data processing as shown in Table 3. ISs 1–4 represent the peaks that are not derived from MA and are used for retention time correction.

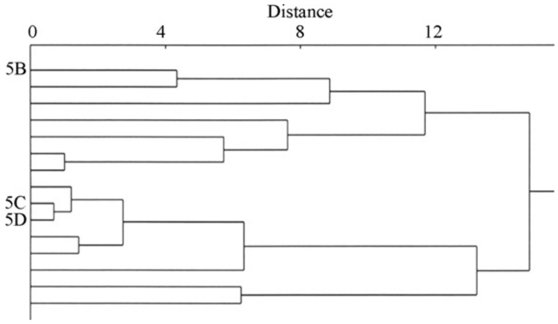

Fig. 6. Dendrogram obtained from a cluster analysis of MA samples in the high-purity group using the SPME method. Fifteen samples in the high-purity group (group A in Fig. 3) were analyzed using the SPME method, and a cluster analysis was performed using seven peaks as shown in Table 3. 5B, 5C and 5D represent samples shown in Fig. 5B–D, respectively.

countries [25,26] has also appeared, a common, global method for profiling MA impurity has not been established yet. If MA samples in different countries were analyzed using the same analytical procedure, and if the data were shared and a global database created, MA impurity profiling would be a more useful tool to investigate international relationships such as drug traffic routes and supply sources.

The automation of data processing in the SPME method was not performed in this study. Although the NRIPS method is now considered sufficient for routine MA impurity profiling, analytical data using the SPME method should also be compiled. In the future, it will be necessary to automate the SPME method as well as the NRIPS method when it becomes difficult to compare and classify samples.

4. Conclusion

Compared to the ONCB method, which is used to profile MA tablet impurities, the NRIPS method is superior for detecting and separating MA impurities. The correction of retention times of impurity peaks with the four ISs made peak identification very accurate for data processing. The 14 peaks selected were characteristic and diagnostic for the comparison and classification of samples.

Sixty-nine samples seized in Japan and 42 in Thailand were analyzed. They were classified into four groups roughly. In addition to LLE, SPME was effective for comparing high-purity MAs because it detected many characteristic peaks.

The combination of LLE and SPME was effective for the comparison and classification of samples from different countries. Adoption of a common analytical method and sharing of data would be useful for investigations of international relationships such as drug traffic routes and supply sources.

Acknowledgments

The authors wish to thank all of the staff at Office of the Narcotics Control Board (ONCB), Thailand, for supplying MA samples and laboratory equipment. The authors also wish to thank Mr. Masahiko Kimura, an expert from the Japan International Cooperation Agency, for his encouragement of this study.

References

[1] National Police Agency of Japan, White Paper on Police, National Police Agency of Japan, Tokyo, 2005, pp. 191–192 (in Japanese).
[2] B. Remberg, A.H. Stead, Drug characterization/impurity profiling, with special focus on methamphetamine: recent work of the United Nations International Drug Control Programme, Bull. Narc. 51 (1999) 97–117.
[3] K. Tanaka, T. Ohmori, T. Inoue, Analysis of impurities in illicit methamphetamine, Forensic Sci. Int. 56 (1992) 157–165.
[4] K. Tanaka, T. Ohmori, T. Inoue, S. Seta, Impurity profiling analysis of illicit methamphetamine by capillary gas chromatography, J. Forensic Sci. 39 (1994) 500–511.
[5] T. Inoue, K. Tanaka, T. Ohmori, Y. Togawa, S. Seta, Impurity profiling analysis of methamphetamine seized in Japan, Forensic Sci. Int. 69 (1994) 97–102.
[6] M. Perkal, Y.L. Ng, J.R. Pearson, Impurity profiling of methamphetamine in Australia and the development of a national drugs database, Forensic Sci. Int. 69 (1994) 77–87.
[7] United Nations International Drug Control Programme (Scientific Section), Scientific and Technical Notes: A practical guide to methamphetamine characterization/impurity profiling: Method procedures, mass spectral data of selected impurities, and literature references, New York, NY, 2000.
[8] M. Lambrechts, T. Klemetsrud, K.E. Rasmussen, H.J. Storesund, Analysis of Leuckart-specific impurities in amphetamine and methamphetamine, J. Chromatogr. 284 (1984) 499–502.
[9] J.H. Liu, W.W. Ku, J.T. Tsay, M.P. Fitzgerald, S. Kim, Approaches to drug sample differentiation. III: A comparative study of the use of chiral and achiral capillary column gas chromatography/mass spectrometry for the determination of methamphetamine enantiomers and possible impurities, J. Forensic Sci. 27 (1982) 39–48.
[10] I.S. Lurie, C.G. Bailey, D.S. Anex, M.J. Bethea, T.D. McKibben, J.F. Casale, Profiling of impurities in illicit methamphetamine by high-performance liquid chromatography and capillary electrochromatography, J. Chromatogr. A 870 (2000) 53–68.
[11] Y.T. Iwata, H. Inoue, K. Kuwayama, T. Kanamori, K. Tsujikawa, H. Miyaguchi, T. Kishi, Forensic application of chiral separation of amphetamine-type stimulants to impurity analysis of seized methamphetamine by capillary electrophoresis, Forensic Sci. Int. 161 (2006) 92–96.
[12] V. Puthaviriyakorn, N. Siriviriyasomboon, J. Phorachata, W. Pan-ox, T. Sasaki, K. Tanaka, Identification of impurities and statistical classification of methamphetamine tablets (Ya-Ba) seized in Thailand, Forensic Sci. Int. 126 (2002) 105–113.
[13] K. Kuwayama, K. Tsujikawa, H. Miyaguchi, T. Kanamori, Y. Iwata, H. Inoue, S. Saitoh, T. Kishi, Identification of impurities and the statistical classification of methamphetamine using headspace solid phase microextraction and gas chromatography–mass spectrometry, Forensic Sci. Int. 160 (2006) 44–52.
[14] K. Kuwayama, H. Inoue, T. Kanamori, K. Tsujikawa, H. Miyaguchi, Y. Iwata, N. Kamo, T. Kishi, Contribution of thermal desorption and liquid–liquid extraction for identification and profiling of impurities in methamphetamine by gas chromatography–mass spectrometry, Forensic Sci. Int., in press.
[15] T. Inoue, S. Suzuki, Studies on metabolism of methamphetamine analogs 6. Analysis of dimethylamphetamine and its metabolites, Rep. Natl. Res. Inst. Police Sci. 39 (1986) 228–234 (in Japanese).
[16] V. Lekskulchai, K. Carter, A. Poklis, W. Soine, GC–MS analysis of methamphetamine impurities: reactivity of (+) or (−)-chloroephedrine and cis- or trans-1,2-dimethyl-3-phenylaziridine, J. Anal. Toxicol. 24 (2000) 602–605.
[17] A.C. Allen, W.O. Kiser, Methamphetamine from ephedrine: I. Chloroephedrines and aziridines, J. Forensic Sci. 32 (1987) 953–962.
[18] H.F. Skinner, Methamphetamine synthesis via hydriodic acid/red phosphorus reduction of ephedrine, Forensic Sci. Int. 48 (1990) 123–134.

[19] T. Kishi, T. Inoue, S. Suzuki, T. Yasuda, T. Oikawa, T. Niwaguchi, Analysis of impurities in methamphetamine, Eisei Kagaku 29 (1983) 400–406 (in Japanese).

[20] H. Inoue, T. Kanamori, Y. Iwata, Y. Ohmae, K. Tsujikawa, S. Saitoh, T. Kishi, Methamphetamine impurity profiling using a 0.32 mm i.d. nonpolar capillary column, Forensic Sci. Int. 135 (2003) 42–47.

[21] T.S. Cantrell, B. John, L. Johnson, A.C. Allen, A study of impurities found in methamphetamine synthesized from ephedrine, Forensic Sci. Int. 39 (1988) 39–53.

[22] J.S. Lee, E.Y. Han, S.Y. Lee, E.M. Kim, Y.H. Park, M.A. Lim, H.S. Chung, J.H. Park, Analysis of the impurities in the methamphetamine synthesized by three different methods from ephedrine and pseudoephedrine, Forensic Sci. Int. 161 (2006) 209–215.

[23] Y. Qi, I. Evans, A. McCluskey, New impurity profiles of recent Australian imported 'ice': methamphetamine impurity profiling and the identification of (pseudo)ephedrine and Leuckart specific marker compounds, Forensic Sci. Int. 169 (2007) 173–180.

[24] F.M. Dayrit, M.C. Dumlao, Impurity profiling of methamphetamine hydrochloride drugs seized in the Philippines, Forensic Sci. Int. 144 (2004) 29–36.

[25] K. Andersson, K. Jalava, E. Lock, et al., Development of a harmonised method for the profiling of amphetamines; III. Development of the gas chromatographic method, Forensic Sci. Int. 169 (2007) 50–63.

[26] K. Andersson, K. Jalava, E. Lock, et al., Development of a harmonised method for the profiling of amphetamines; IV. Optimisation of sample preparation, Forensic Sci. Int. 169 (2007) 64–76.