Environ. Sci. Technol. **2005**, *39,* 8442−8447

Matrix-Assisted Laser Desorption/ Ionization Time-of-Flight Mass Spectrometry with a Matrix of Carbon Nanotubes for the Analysis of Low-Mass Compounds in Environmental Samples

LIGANG HU,[†,‡] SONGYUN XU,[‡] CHENSONG PAN,[‡] CHUNGANG YUAN,[†] HANFA ZOU,[*,†] AND GUIBIN JIANG[*,†]

State Key Laboratory of Environmental Chemistry and Ecotoxicology, Research Center for Eco-Environmental Sciences, Chinese Academy Sciences, Beijing 100085, China, and National Chromatographic R&A Center, Dalian Institute of Chemical Physics, Chinese Academy Sciences, Dalian 116023, China

The use of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) for environmental analysis has been mainly focused on qualitative analysis of high-mass molecules, such as toxins, humic acid, and microorganisms. Herein, we describe a novel MALDI-TOF-MS method with a matrix of oxidized carbon nanotubes for analysis of low-mass compounds in environmental samples. A number of chemicals in the environment were qualitatively analyzed by the present method, and it was found that most of them, especially the highly polar chemicals, were measurable with high sensitivity. With the intrinsic ability to measure high-mass chemicals, this method can compensate for the current shortage of methods for environmental analysis for the measurement of highly polar or high-mass chemicals. For sample analysis, arsenic speciation in Chinese traditional medicines was qualified and diphenylolpropane in water samples was quantified. With the relatively high tolerance of the method to interfering molecules, a simple pretreatment or even no pretreatment could be employed before MS detection. Furthermore, this method can be employed in a high-throughput format.

Introduction

Mass spectrometry, including gas chromatography/mass spectrometry (GC/MS), liquid chromatography/mass spectrometry (LC/MS), and inductively coupled plasma mass spectrometry (ICPMS), has been widely applied in environmental analysis, and an increased coupling of different extraction and separation methods with these detection methods was developed recently (*1*−*3*). As a powerful tool to characterize biomolecules and polymers (*4*−*7*), matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) has been applied primarily in the life sciences. For environmental analysis, this method has been used to probe the structures of natural, high-molecular-weight organic substances (i.e., humic acid) (*8*). Also, MALDI-TOF-MS has been employed increasingly in the analysis of microorganisms. It has not only been used for simple fingerprinting analysis (*9*, *10*) but modeling approaches for improving identifications and complete sequencing of protein biomarkers of these microorganisms also have been developed (*11*−*13*). However, for the low-mass molecules, matrix ion interface and detector saturation were inevitable in MALDI-TOF-MS with traditional organic matrixes, which made the characterization of small molecules obscured and difficult. Carbon nanotubes were introduced as a matrix for MALDI-TOF-MS in 2003, which succeeded at almost eliminating the background ion interference and offered a new technology for high-speed analysis of low-mass compounds (*14*, *15*).

The poor solubility of the raw carbon nanotubes made it difficult for them to be deposited onto the sample target for the formation of a homogeneous layer, which directly led to the poor reproducibility and resolution of the low-mass analytes. Also, the contained impurities (i.e., amorphous carbon, graphite pieces, and catalytic metal particles) in the raw carbon nanotubes could interrupt their functions as the energy receptacle for laser radiation and the energy transporter for the analytes (*16*).

Recently, functionalized carbon nanotubes have attracted more and more attention because of their interesting capabilities in different applications (*17*−*20*). MALDI-TOF-MS with oxidized carbon nanotubes as the matrix has been developed for low-mass molecule analysis in biological samples. After an oxidization procedure, carbon nanotubes become purified and water-soluble. As a result, simpler sample-handling procedures were realized, and good reproducibility of intra- and intersample spots was obtained, which made quantitative analysis with this method possible. Here, we applied this method to analyze low-mass analytes in environmental samples. A number of chemicals, including organotin, organoarsenic, organophosphate, organomecury, alkyl phenol, polycyclic aromatic hydrocarbons (PAHs), aniline and its derivates, atrazine derivates, naphthol derivatives, humic acid, etc., have been applied to evaluate the validity of this method. It was found that polar and nonvolatile chemicals could be detected well. Furthermore, with the ability to detect high-molecular-weight compounds, this method may simultaneously measure the highly polar and high-molecular-weight compounds presented in environmental samples, which were difficult to detect with traditional methods based on gas chromatography. Without the tedious separation step, MALDI-TOF-MS was simple and rapid and could be employed in a high-throughput format. For experimental samples, arsenic speciations in Chinese traditional medicines were qualified and diphenylolpropane (BPA) in water samples was quantified.

2. Experimental Section

2.1. Instrumentation. The mass spectrometry measurements were performed with an Autoflex (Bruker Doltonics, Germany) MALDI-TOF mass spectrometer equipped with a pulsed nitrogen laser (337 nm) at a frequency of 20 Hz. A ground-steel sample target with 384 spots was employed in our experiments. The diameters of the spots were 4 mm, but the deposited sample could not cover the whole spot, and the diameters of the sample spots were generally about 2 mm. Ions were desorbed from the surfaces of carbon nanotubes with laser energies of about 75 μJ per pulse. The

* Address correspondence to either author. Phone: 86-10-62849334 (G.J.); 86-411-84379610 (H.Z.). Fax: 86-10-62849179 (G.J.); 86-411-84379620 (H.Z.). E-mail: gbjiang@mail.rcees.ac.cn (G.J.); hanfazou@dicp.ac.cn (H.Z.).

† Research Center for Eco-Environmental Sciences.

‡ Dalian Institute of Chemical and Physics.

10.1021/es0508572 CCC: $30.25
Published on Web 10/04/2005

measurements were performed in positive and negative ionization reflection modes, because the linear mode was not suitable for quantitative analysis.

2.2. Chemicals and Materials. All reagents were analytical-grade unless mentioned otherwise. Multiwalled carbon nanotubes were kindly offered by Professor F. Wei (Tsinghua University, Beijing, China), and BDE209 was kindly provided by Dr. Qinghua Zhang (Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences). Dimethyl formamide and methanol were purchased from Kermel Chemicals (Tianjin, China). The Chinese traditional medicines were purchased from a local Chinese medicine store. All of the chemicals and solutions for qualitative analysis were purchased from J&K Chemicals (Beijing, China). The water used in the experiments was prepared by a Milli-Q system (Millipore, Milford, MA)

2.3. Procedure for Oxidation of Carbon Nanotubes. The raw carbon nanotubes offered by Professor Wei, which were synthesized by the catalytic chemical vapor deposition method, were 10 nm in outer diameter, about 3−5 nm in inner diameter, and more than several micrometers in length (*21*). After oxidation, the carbon nanotubes were cut into thinner, rougher, and shorter pieces with the carboxylic groups on their surfaces. The procedure for the oxidation of carbon nanotubes has been described in our previous paper (*16*). Briefly, 200 mg of carbon nanotubes was placed into the mixture of concentrated HNO_3 and H_2SO_4 (v/v, 1:3) by stirring and refluxing at 120 °C for 30 min. Then the solution was cooled to room temperature, diluted to 300 mL with water, filtered through a 0.45 μm membrane, and rinsed with water until the pH value approached 7.0. The oxidized carbon nanotubes with the membrane were transferred into 50 mL of ethanol, and after sonication for 1 min the membrane was removed from the solution of oxidized carbon nanotubes in the ethanol. After ethanol was carefully heated to boil and evaporated, about 30 mg of oxidized carbon nanotubes was collected and stored in dry conditions for further usage.

2.4. Preparation of Analyte Solutions. Anthracene, phenanthrene, chrysene, fluorene, BPA, nonylphenol, octylphenol, decabromodiphenyl oxide, 3,4-xylidine, 4-chloroaniline, 2,4-dichloroaniline, 2,4,6,-trichloroaniline, 2-nitroso-1-naphthol, 1-(2-pyridylazo)-2-naphthol, 2-naphthol-3,6-disulfonic acid salt, phenyltin trichloride, diphenyltin dichloride, triphenyltin chloride, butyl trichlorotin, dibutyl dichlorotin, trichloromethylstannane, trimethyltin chloride, dimethyltin dichloride, dibutyltin dilaurate, tributylchlorostannane, and methyl mercury chloride were dissolved in dimethylformamide (DMF) at a concentration of 1.0 mg/mL. Diquat, paraquat, malathion, methamidphos, parathion, and phorate were dissolved in a solution of methanol/water (1:1) at a concentration of 0.05 mg/mL. Chlormequat chloride was dissolved in a solution of acetonitrile/water (1:1) at a concentration of 0.05 mg/mL. Methane arsenate (MMA), cacodylic acid (DMA), arsenous acid, and arsenic acid were dissolved in water at a concentration of 1.0 mg/mL. Arsenobetaine (AsB) was dissolved in water at a concentration of 0.4 mg/mL, and arsenocholine (AsC) was dissolved in water at a concentration of 0.225 mg/mL. Humic acid was saturated in a solution of methanol/water (1:1), and 1-amino-2-naphthol-4-sulfonic acid, tetraphenyl tin, and dioctyltin oxide were saturated in DMF.

The solutions for quantitative analysis were diluted from the stock solutions step by step, respectively. All solutions were stored in a refrigerator at approximately 4 °C for further usage.

2.5. Preparation of Extracts of Chinese Traditional Medicines. A 1.0 g sample was extracted with 10 mL of water/methanol (v/v, 1:1). Each extraction required vortex mixing, 30 min of sonication, and 15 min of centrifugation at 3500 rpm. The supernatant was collected in a polytetrafluoroethylene (PTFE) bottle, and the procedure was repeated twice with 5 mL of reagent. Finally, the supernatants were combined. The solvent of the combined extract was removed by rotary evaporation, and the residue (nearly dry) was redissolved to a final volume of 10.0 mL with deionized water. The extract were filtered through 0.2 μm membrane filters before usage.

2.6. Procedure for Quantitative Determination of BPA in Water Samples. A tap water sample was collected from the water tap in our laboratory. A seawater sample was collected from the Dalian coast area in the Yellow Sea. Wastewater 1 and wastewater 2 were collected from the Malan River and the Dalian Economic and Technological Development Area in Dalian, respectively. The collected water samples were filtered through a 0.45 μm membrane immediately after sampling and were kept in glass containers, then stored at a temperature of 4 °C.

The outlet tip of a C_{18} cartridge (0.5 g, 5 mL) was connected to a solid-phase extraction system (Tengda Corporation, Tianjin, China), the inlet end of the cartridge was connected to a PTFE suction tube, and the other end was inserted into a sample solution. Before usage, the entire solid-phase extraction assembly was carefully washed with sufficient methanol.

Prior to the preconcentration step, the C_{18} cartridge was preconditioned by washing with 5 mL of methanol and activated with 5 mL of water. The pH value of the samples was adjusted to approximately 7.0 with 1.0 M of sodium hydroxide or hydrochloric acid solution. Then 500 mL of a water sample was passed through the cartridge at a flow rate of 10 mL/min. After that, the cartridge was washed with 5 mL of water to remove coadsorbed materials from the cartridge. Then the analyte was eluted with 4 mL methanol, and the eluate was concentrated to 0.1 mL with a rotary vacuum evaporator at 40 °C.

2.7. Sample Preparation for MALDI-TOF-MS. The matrix solution of oxidized carbon nanotubes was prepared at a concentration of approximately 1.0 mg/mL in methanol/water (1:1) solution. A 1.0−2.0 μL solution of oxidized carbon nanotubes, which would form a thin layer in few minutes by evaporation of the solvent, was dispensed onto the target. Then 0.5−1.0 μL of the solution of the analyte was dispensed onto the layer of matrix, left in the air for few minutes to evaporate the solvent, and then analyzed by MALDI-TOF-MS.

2.8. Quantitative Analysis. For each sample, spectra representing the sum of 300 laser shots each were obtained from three different sample spots. The ratios of the peak intensity of the analyte relative to the internal standards were calculated with an average value of three measurements for each concentration. Calibration curves were constructed by plotting the averaged ratios of the analyte to the calibrant peak intensity as a function of added BPA quantity with linear regression analysis.

3. Results and Discussion

A series of environmentally relevant compounds were collected and detected by MALDI-TOF-MS, which included organotin, organoarsenic, organophosphate, organomecury, alkyl phenol and BPA, PAHs, anilines, atrazine derivatives, naphthol derivatives, chlormequat chloride, diquat, paraquat, humic acid, and decabromodiphenyl oxide (BDE209). The concentrations of these compounds were approximately 1.0 mg/mL, except humic acid, 1-amino-2-naphthol-4-sulfonic acid, tetraphenyl tin, and dioctyltin oxide because of their poor solubilities and organophosphates, chlormequat chloride, diquat, paraquat, arsenobetaine, and arsenocholine because of their low concentrations in the stock solutions. The obtained results are shown in Table 1.

TABLE 1. Results Obtained in Positive Reflection Mode[a]

chemical	concentration[b] (mg/mL)	amount[b] (nmol)	peak intensity[c] (detected in positive reflection mode)	peak intensity[c] (detected in negative reflection mode)
3,4-xylidine	1.0	4.1	150	0
4-chloroaniline	1.0	3.9	0	0
2,4-dichloroaniline	1.0	3.1	0	0
2,4,6-trichloroaniline	1.0	2.5	0	0
2-nitroso-1-naphthol	1.0	2.9	1226	3353
1-(2-pyridylazo)-2-naphthol	1.0	1.7	1575	4737
1-amino-2-naphthol-4-sulfonic acid	S	U	0	2913
2-naphthol-3,6-disulfonic acid disodium salt	1.0	1.4	0	181
phenyltin trichloride	1.0	1.6	0	1708
diphenyltin dichloride	1.0	1.4	0	1467
triphenyltin chloride	1.0	1.3	217	1288
tetraphenyl tin	S	U	0	619
butyl trichlorotin	1.0	1.8	0	1088
dibutyl dichlorotin	1.0	1.6	0	267
trichloromethylstannane	1.0	2.1	0	398
trimethyltin chloride	1.0	2.5	0	0
dimethyltin dichloride	1.0	2.3	0	0
dioctyltin oxide	S	U	0	0
dibutyltin dilaurate	1.0	0.8	536	123
tributylchlorostannane	1.0	1.5	0	0
2-hydroxy atrazine	0.05	0.1	255	236
desisopropylatrazine	0.05	0.1	101	157
atrazine-desisopropyl-2-hydroxy	0.05	0.2	466	458
desethylatrazine	0.05	0.1	110	127
anthracene	1.0	2.8	149	0
phenanthrene	1.0	2.8	125	0
chrysene	1.0	2.2	318	146
9H-fluorene	1.0	3.0	0	0
malathion	0.05	0.08	518	0
methamidphos	0.05	0.2	254	198
parathion	0.05	0.08	454	0
phorate	0.05	0.1	126	0
methyl mercury chloride	1.0	2.0	0	0
diphenylolpropane	1.0	2.2	0	2848
nonylphenol	1.0	2.3	0	291
octylphenol	1.0	2.4	0	262
cacodylic acid	1.0	3.6	1755	4575
methane arsenate	1.0	3.6	1623	3800
arsenobetaine	0.4	1.1	5072	0
arsenocholine	0.225	0.07	6788	2283
aresenous acid	1.0	4.0	2728	0
arsenic acid	1.0	3.5	1005	0
diquat	0.05	0.1	2650	0
paraquat	0.05	0.1	1606	0
chlormequat chloride	0.05	0.2	1147	0
humic acid	S	U	206	0
BDE209	1.0	0.5	0	947

[a] S, saturated solution; U, unknown. [b] The concentration and the amount are the concentration and the amount of analyte solutions that were deposited onto the carbon nanotubes, respectively. [c] The listed peak intensity is the greatest intensity of the observed peak.

It was found that polar and nonvolatile chemicals could be detected well. Especially for highly polar compounds such as diquat, paraquat, DMA, MMA, AsB, AsC, etc., very low limits of detection could be achieved. For example, the detection limit of paraquat could reach 0.5 pg (with a signal-to-noise ratio >3). The high-mass compounds such as BDE209 also could be detected well. These two characteristics could be beneficial for the measurement of highly polar and high-mass compounds present in an environmental sample, which are not detected well with methods based on GC (*3*). Because a vacuum step was employed during the sample target entering the ion source, compounds with a high vapor pressure would be hard to detect due to volatilization.

With the automated unattended sample throughput (the designed throughput for the Autoflex, which was used in our experiments, is more than 30 000 samples per cycle), high-throughput analysis could be easily realized with the described method. After the sample was deposited, the detection proceeded in the unattended automated mode. With this advantage, the described method with the Autoflex mass spectrometer or similar instruments could be employed as a screening method of analysis in applications such as environmental pollutant monitoring, health and safety protection, and control of additives and other substances present in food, especially when dealing with huge numbers of samples.

3.1. Arsenic Speciation in Chinese Traditional Medicines. The methods for arsenic speciation analysis usually have employed a tedious separation step before detection (*22*, *23*). GC and LC were the most commonly employed methods, and different species could be identified by different retention times. In MALDI-TOF-MS, multiple compounds could be detected simultaneously and identified by their respective molecular weight. Compounds with different molecular weights could be easy to distinguish by MALDI-TOF-MS. Therefore, for the experimental sample with a relatively simple matrix, MALDI-TOF-MS with a matrix of carbon nanotubes could be a simple and fast method for species

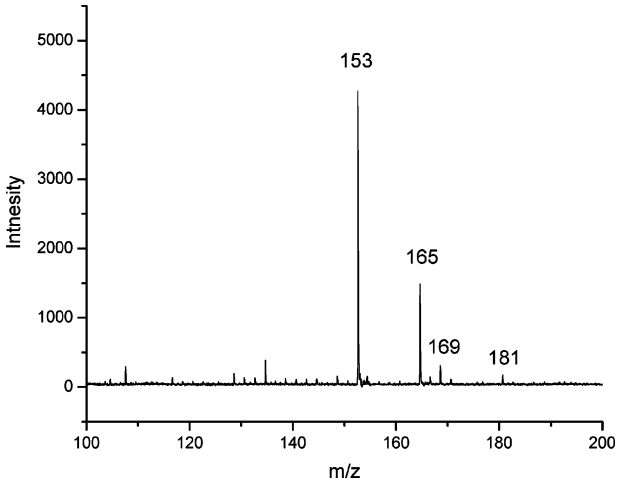

FIGURE 1. Mass spectrum for a solution containing As(III) and As(V) detected in positive reflection mode.

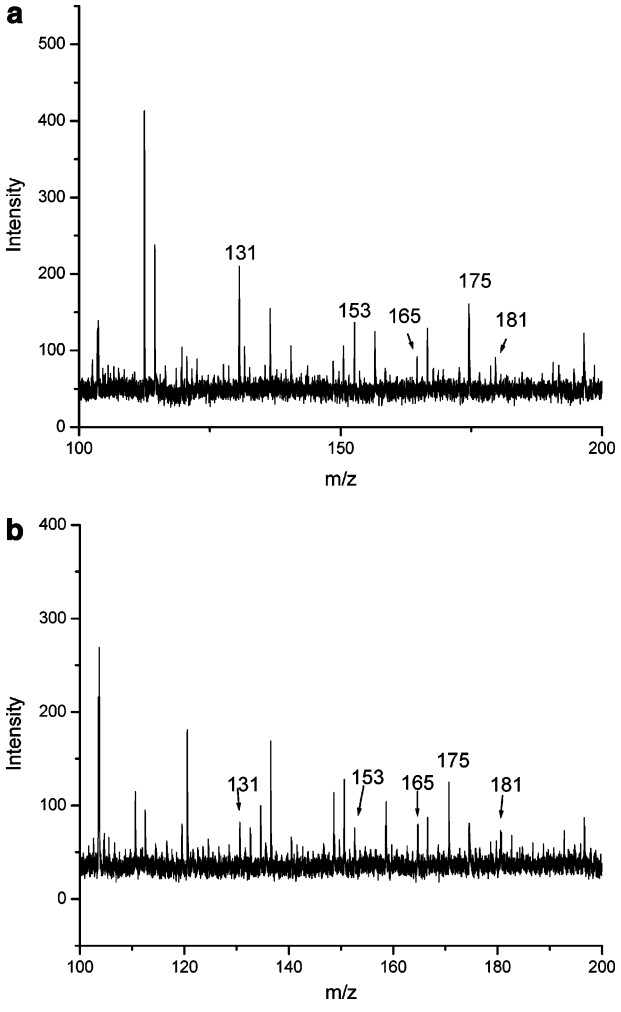

FIGURE 2. (a) Mass spectrum for Chinese traditional medicine 1 detected in positive reflection mode. (b) Mass spectrum for Chinese traditional medicine 2 detected in positive reflection mode.

analysis. Figure 1 shows the spectrum of a mixture solution containing As(III) and As(V) measured in positive reflection mode. The peaks at m/z of 153 and 169 are the $[HAsO_2 + 2Na - H]^+$ and $[HAsO_2 + Na + K - H]^+$ ions, and the peaks at m/z of 165 and 181 are the $[H_3AsO_4 + Na - H]^+$ and $[H_3AsO_4 + K - H]^+$ ions. The different arsenic species were detected simultaneously and would not be confused for different peaks.

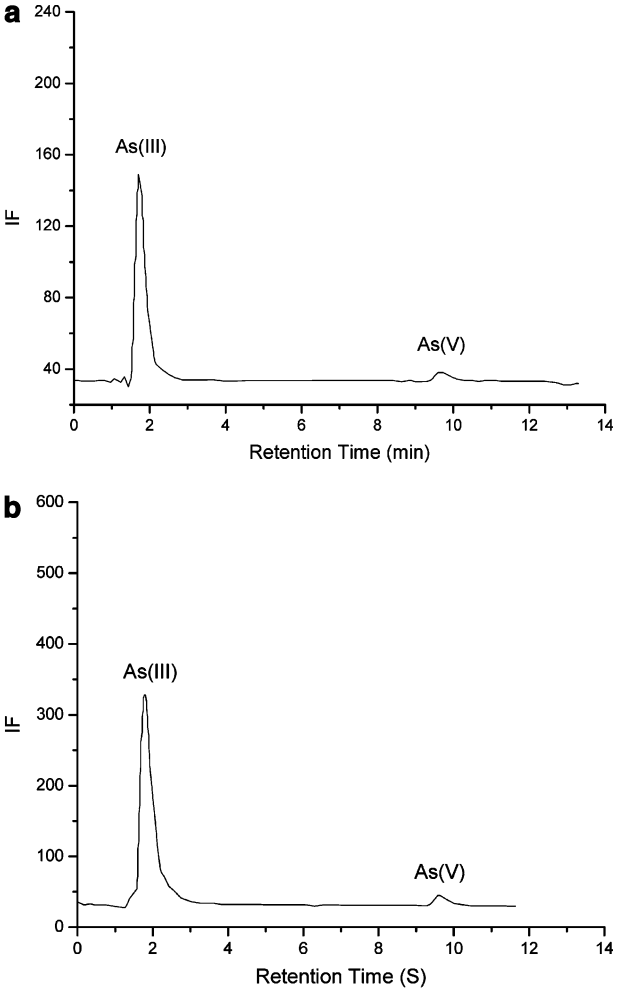

FIGURE 3. (a) Chromatograph for Chinese traditional medicine 1 measured by HPLC-HG-AFS with a Dionex IonPac AS11 column (250 mm × 4.0 mm i.d.). Mobile phase: A, H_2O; B, 100 mmol L^{-1} solution of NaOH; 0−5 min, 90% A, 10% B; 5−6 min, 90−0% A, 10−100% B; 6−10 min, 100% B; 10−11 min, 0−90% A, 100−10% B. (b) Chromatograph for Chinese traditional medicine 2 measured by HPLC-HG-AFS with a Dionex IonPac AS11 column (250 mm × 4.0 mm i.d.). Mobile phase: A, H_2O; B, 100 mmol L^{-1} solution of NaOH; 0−5 min, 90% A, 10% B; 5−6 min, 90−0% A, 10−100% B; 6−10 min, 100% B; 10−11 min, 0−90% A, 100−10% B.

Because this method has a high tolerance to disturbance, the two extracts of Chinese traditional medicines were directly detected without any further separation and purification. Figures 2a and 2b show the mass spectrum obtained from the extracts of Chinese traditional medicines 1 and 2, respectively. It is obvious that peaks for $HAsO_2$ (131, $[M + Na]^+$; 153, $[M + 2Na - H]^+$; 175, $[M + Na + K - H]^+$) and H_3AsO_4 (165, $[M + Na]^+$; 181, $[M + K]^+$) were detected in these two Chinese traditional medicines, which are consistent with the results obtained by high-performance liquid chromatograph (HPLC). The results measured by the HPLC method are shown in Figures 3a and 3b. Because of the high concentrations of salts in the two extracts, a wash step with water on the target was employed to desalt, because the salts could interfere with the detection seriously. The arsenic in these two Chinese traditional medicines probably comes from the bezoar that is one of the components of the two Chinese traditional medicines. Certainly, a purification step before detection is appropriate for samples with a complex matrix.

3.2. Quantitative Analysis for BPA. MALDI-TOF-MS mainly has been applied for qualitative analysis of biomolecules and other high-molecular-weight compounds. Re-

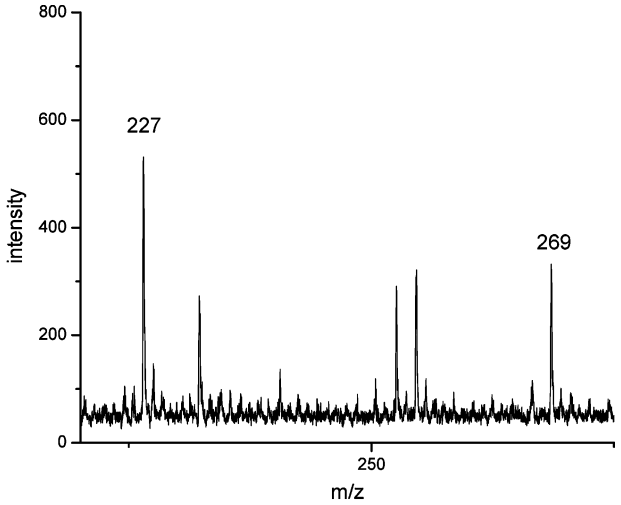

FIGURE 4. Typical mass spectrum for BPA and estrone detected in negative reflection mode.

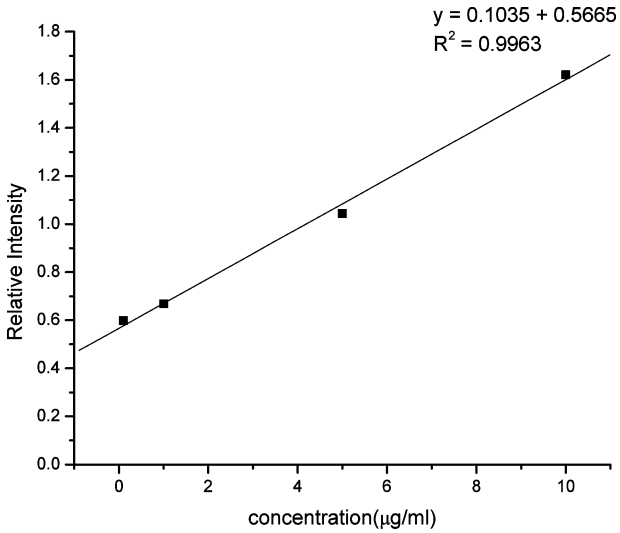

FIGURE 5. Calibration curves for quantitative analysis of BPA.

cently, several methods based on MALDI-TOF-MS were developed for low-mass compound analysis (*24*, *25*). Because of the heterogeneity of analyte crystallization and the variation of the irradiation laser between shot to shot, an isotope-labeled analyte molecule or a molecule structurally analogous to the analyte was used as the internal standard for quantitative analysis in MALDI-TOF-MS. Although good reproducibility of intra- and intersample spots was obtained by MALDI-TOF-MS with a matrix of oxidized carbon nanotubes, internal standards were employed in our experiment for quantitative analysis of BPA by MALDI-TOF-MS, and estrone was chosen as an internal standard.

Figure 4 shows a typical mass spectrum for BPA quantitative analysis acquired in negative reflection mode. The peaks at m/z of 227 and 269 are the peaks of $[M - H]^-$ for BPA and estrone, respectively. Calibration curves were obtained for both peak intensity and area ratios. Peak area ratios were slightly more linear than intensity ratios when the BPA concentration ranged from 10 to 500 μg/mL, but the results were reversed when the BPA concentration ranged from 0.1 to 10 μg/mL. Because the concentration of BPA in the experimental samples was always very low, intensity ratios were selected for calibration curves in our experiment. Also, two sample preparation procedures were compared. The difference between these two procedures varied in the order of adding the internal standards. One was that the solutions of internal standards were deposited onto the matrix of oxidized carbon nanotubes before the solutions of analyte were deposited, and another was that the solutions of the internal standards were mixed with the solutions of the analyte previously and then deposited together. No obvious differences were observed between the two procedures according to the coefficients of correlation and slope of the calibration curve. The first procedure was selected for its convenience in handling of the samples. Figure 5 shows the calibration curves for BPA quantitative analysis, and a good linear correlation was obtained with $R^2 = 0.9963$. The concentration of BPA in the solution was varied from 0.1 to 10 μg/mL, and the concentration of the internal standard was kept constant at 10 μg/mL. For a high-concentration solution of BPA, a higher concentration of the internal standard should be chosen.

The proposed method was applied to the quantitative analysis of BPA in environmental water samples, and the results are shown in Table 2. A high concentration of BPA was found in the sample collected from the Dalian Development Area. Recovery tests were carried out with water samples spiked with BPA, and the recovery ranged from 92% to 110%.

TABLE 2. Results for Quantitative Analysis of BPA in Water Samples

sample	concentration (ng/mL)	recovery (%)
seawater	not detected	
seawater + 0.80 ng/mL	0.740	95.4
wastewater 1	not detected	
wastewater 1 + 0.80 ng/mL	0.812	102.0
wastewater 2	8.172	
wastewater 2 + 0.80 ng/mL	9.048	109.5
tap water	not detected	
tap water + 0.80 ng/mL	0.763	92.5

In comparison to GC (*26*) and HPLC (*27*, *28*) methods for quantitative analysis of BPA, MALDI-TOF-MS gives the advantage of rapidness and simplicity for total quantification. Especially for a sample in a relatively simple matrix, high-throughput analysis could be achieved easily. With the advantages of high sample throughout and unattended automation, the described method could be employed as a screening method of analysis in applications such as environmental pollutant monitoring, health and safety protection, and control of additives and other substances present in food, especially when dealing with huge numbers of samples.

Acknowledgments

This work was jointly supported by the National Basic Research Program of China (Grant No. 2003CB415001) and the State High Tech Development Plan (Grant No. 2003AA640610).

Literature Cited

(1) Richardson, S. D. Environmental Mass Spectrometry. *Anal. Chem.* **2000**, *72*, 4477−4496.
(2) Richardson, S. D. Environmental Mass Spectrometry: Emerging Contaminants and Current Issues. *Anal. Chem.* **2002**, *74*, 2719−2742.
(3) Richardson, S. D. Environmental Mass Spectrometry: Emerging Contaminants and Current Issues. *Anal. Chem.* **2004**, *76*, 3337−3364.
(4) Liang, X.; Bai, J.; Liu, Y.-H.; Lubman, D. M. Characterization of SDS-PAGE-Separated Proteins by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry. *Anal. Chem.* **1996**, *68*, 1012−1018.
(5) Butler, J. M.; Jiang-Baucom, P.; Huang, M.; Belgrader, P.; Girard, J. Peptide Nucleic Acid Characterization by MALDI-TOF Mass Spectrometry. *Anal. Chem.* **1996**, *68*, 3283−3287.

(6) Annan, R. S.; Carr, S. A. Phosphopeptide Analysis by Matrix-Assisted Laser Desorption Time-of-Flight Mass Spectrometry. *Anal. Chem.* **1996**, *68*, 3413−3421.
(7) Williams, J. B.; Gusev, A. I.; Hercules, D. M. Characterization of Polyesters by Matrix-Assisted Laser Desorption Ionization Mass Spectrometry. *Macromolecules* **1997**, *30*, 3781−3787.
(8) Gajdosova, D.; Novotna, K.; Prosek, P.; Havel, J. Separation and Characterization of Humic Acids from Antarctica by Capillary Electrophoresis and Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry Inclusion Complexes of Humic Acids with Cyclodextrins. *J. Chromatogr., A* **2003**, *1014*, 117−127.
(9) Welker, M.; Fastner, J.; Erhard, M.; Dohren, H. V. Applications of MALDI-TOF MS Analysis in Cyanotoxin Research. *Environ. Toxicol.* **2002**, *17*, 367−374.
(10) Karlsson, K.; Sipia, V.; Krause, E.; Meriluoto, J. Mass Spectrometric Detection and Quantification of Nodularin-R in Flounder Livers. *Environ. Toxicol.* **2003**, *18*, 284−288.
(11) Stump, M. J.; Jones, J. J.; Fleming, R. C.; Lay, J. O.; Wilkins, C. L. Use of Double-Depleted ^{13}C and ^{15}N Culture Media for Analysis of Whole Cell Bacteria by MALDI Time-of-flight and Fourier Transform Mass Spectrometry. *J. Am. Soc. Mass Spectrom.* **2003**, *14*, 1306−1314.
(12) Pineda, F. J.; Antoine, M. D.; Demirev, P. A.; Feldman, A. B.; Jackman, J.; Longenecker, M.; Lin, J. S. Microorganism Identification by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry and Model-Derived Ribosomal Protein Biomarkers. *Anal. Chem.* **2003**, *75*, 3817−3822.
(13) Yao, Z.-P.; Afonso, C.; Fenselau, C. Rapid Microorganism Identification with On-Slide Proteolytic Digestion Followed by Matrix-Assisted Laser Desorption/Ionization Tandem Mass Spectrometry and Database Searching. *Rapid Commun. Mass Spectrom.* **2002**, *16*, 1953−1956.
(14) Xu, S.; Li, Y.; Zou, H.; Qiu, J.; Guo, Z.; Guo, B. Carbon Nanotubes as Assisted Matrix for Laser Desorption/Ionization Time-of-Flight Mass Spectrometry. *Anal. Chem.* **2003**, *75*, 6191−6195.
(15) Pan, C.; Xu, S.; Zou, H.; Guo, Z.; Zhang, Y.; Guo, B. Carbon Nanotubes as Adsorbent of Solid-Phase Extraction and Matrix for Laser Desorption/Ionization Mass Spectrometry. *J. Am. Soc. Mass Spectrom.* **2005**, *16*, 263−270.
(16) Pan, C.; Xu, S.; Hu, L.; Su, X.; Ou, J.; Zou, H.; Guo, Z.; Zhang, Y.; Guo, B. Using Oxidized Carbon Nanotubes as Matrix for Analysis of Small Molecules by MALDI-TOF MS. *J. Am. Soc. Mass Spectrom.* **2005**, *16*, 883−892.
(17) Chen, J.; Hamon, M. A.; Hu, H.; Chen, Y. S.; Rao, A. M.; Eklund, P. C.; Haddon, R. C. Solution Properties of Single-Walled Carbon Nanotubes. *Science* **1998**, *282*, 95−98.
(18) Fu, K. F.; Sun, Y. P. Dispersion and Solubilization of Carbon Nanotubes. *J. Nanosci. Nanotechnol.* **2003**, *3*, 351−364.
(19) Ugarov, M. V.; Egan, T.; Khabashesku, D. V.; Schultz, J. A.; Peng, H.; Khabashesku, V. N.; Furutani, H.; Prather, K. S.; Wang, H.-W. J.; Jackson, S. N.; Woods, A. S. MALDI Matrices for Biomolecular Analysis Based on Functionalized Carbon Nanomaterials. *Anal. Chem.* **2004**, *76*, 6734−6742.
(20) Chen, W.-Y.; Wang, L.-S.; Chiu, H.-T.; Chen, Y.-C.; Lee, C.-Y. Carbon Nanotubes as Affinity Probes for Peptides and Protein in MALDI MS Analysis. *J. Am. Soc. Mass Spectrom.* **2004**, *15*, 1629−1635.
(21) Wang, Y.; Wei, F.; Luo, G.; Yu, H.; Gu, G. The Large-Scale Production of Carbon Nanotubes in a Nano-Agglomerate Fluidized-Bed Reactor. *Carbon* **2002**, *364*, 568−572.
(22) Madsen, A. D.; Gossler, W.; Pederson, S. N.; Francesconi, K. A. Characterization of an Algal Extract by HPLC-ICP-MS and LC-Electrospray MS for Use in Arsenosugar Speciation Studies. *J. Anal. At. Spectrom.* **2000**, *15*, 657−662.
(23) Hulle, M. V.; Zhang, C.; Zhang, X.; Cornelis, R. Arsenic Speciation in Chinese Seaweeds Using HPLC-ICP-MS and HPLC-ES-MS. *Analyst* **2002**, *127*, 634−640.
(24) Thomas, J. J.; Shen, Z.; Crowell, J. E.; Finn, M. G.; Siuzdak, G. Desorption/Ionization on Silicon (DIOS): A Diverse Mass Spectrometry Platform for Protein Characterization. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 4932−4937.
(25) Guo, Z.; Zhang, Q.; Zou, H.; Guo, B.; Ni, J. A Method for Analysis of Low-Mass Molecules by MALDI-TOF Mass Spectrometry. *Anal. Chem.* **2002**, *74*, 1637−1641.
(26) Shin, H.-S.; Park, C. −H.; Park, S. -J.; Pyo, H. Sensitive Determination of Bisphenol A in Environmental Water by Gas Chromatography with Nitrogen−Phosphorus Detection after Cyanomethylation. *J. Chromatogr., A* **2001**, *912*, 119−125.
(27) Sun, Y.; Irie, M.; Kishikawa, N.; Wada, M.; Kuroda, N.; Nakashima, K. Determination of Bisphenol A in Human Breast Milk by HPLC with Column-Switching and Fluorescence Detection. *Biomed. Chromatogr.* **2004**, *18*, 501−507.
(28) D'Antunono, A.; Dall'Orto, V. C.; Balbo, A. L.; Sobral, A.; Rezzano, I. Determination of Bisphenol A in Food-Stimulating Liquids Using LCED with a Chemically Modified Electrode. *J. Agric. Food Chem.* **2001**, *49*, 1098−1101.

Received for review May 4, 2005. Revised manuscript received August 17, 2005. Accepted September 1, 2005.

ES0508572