Lithium Ion Attachment Mass Spectrometry for the Direct Detection of Organoarsenic Compounds in the Metallomics Studies

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In this study, three organoarsenic compounds including dimethylarsinic acid, trimethylarsine oxide, and arsenic ethoxide were directly detected by coupling a direct sample insertion probe with a lithium ion attachment mass spectrometer. Previously only gaseous sample could be detected by this method; however, solid and liquid samples can also be detected directly with the use of a direct sample insertion probe. This method will be applicable for the direct analysis of various organometallic compounds in the latest metallomics studies.

Metallomics is a new scientific field, which is proposed after the genomics, proteomics and metabollomics.[1] The main research target of metallomics proposed by Haraguchi is the identification of metallomes and the elucidation of their biological or physiological functions in the biological systems. Chemical speciation for specific identification of bioactive metallomes is one of the most important analytical technologies to establish metallomics as the integrated biometal science.[2] In the past, the complicated biological system was usually explained by determining the total content of the elements involved in the system. Obviously it is not comprehensive because the metal ion functions and toxic effects are tightly related to their concentrations, as well as their chemical form. So, chemical speciation or elemental speciation has received extensive study in recent years.[3–6] Generally, arsenic is an essential element in animals and probably in man, and some forms of arsenic are toxic at certain levels. Their toxicity varies greatly because of different speciation, for example, monomethyl arsonate (MMA) and dimethylarsinate are about 1000 times more toxic than arsenobetaine (AB).[7] Therefore, it is necessary to assess environmental risks and understand their biological functions by the approach of chemical speciation adequately.[8,9]

Up to now, many analytical techniques were developed for chemical speciation of trace metals in the biological samples, such as liquid chromatography with inductively coupled plasma mass spectrometry (LC-ICP-MS), gas chromatography with inductively coupled plasma mass spectrometry (GC-ICP-MS), and liquid chromatography inductively coupled plasma mass spectrometry with atomic emission spectrometry (LC-ICP-AES). For the speciation of arsenic compounds, LC-ICP-MS has been used mainly.[10,11] However, this method has a fundamental limitation that identification of metal compounds is based solely on the matching of retention times. As a consequence, errors can result from using this approach, especially in cases of coeluting metal species. Furthermore, lack of appropriate standards could prevent identification altogether.[12] To resolve these problems, recently the use of LC with electrospray mass spectrometry (LC-ES-MS) has been reported.[13] As a soft ionization method, LC-ES-MS can identify arsenic compounds by retention time and mass spectrum together. However, it also needs separation approach such as LC before mass spectrometry. Thus, a method is required to detect arsenic compounds directly and quickly.

Ion attachment mass spectrometry (IAMS) is a developed ionization method that the whole molecule ion is produced through lithium ion attaching to a sample molecule. With IAMS a soft ionization technique, compound's structure cannot be destroyed. Only one molecular peak per one ingredient appears on a mass spectrum.[14–18] So no separation approach is needed in IAMS. However, only gaseous sample could be ionized and detected by IAMS. The method is desired to develop so that solid and liquid sample can also be detected. Therefore, we developed a new method by coupling a direct sample insertion probe with lithium ion attachment mass spectrometry (DIP-IAMS). DIP is a kind of sample inlet system that liquid and solid samples can be heated and gasified quickly, and then the gasified samples are directly introduced into the high vacuum.[19] With this method, no separation approach is needed, and direct determination of solid and liquid sample is also possible. In this study, by using this method several organoarsenic compounds, e.g., dimethylarsinic acid (DMAA), trimethylarsine oxide (TMAO), and arsenic ethoxide (AsE) were detected directly.

DMAA, TMAO, and AsE of HPLC grade were purchased from Kanto Chemical Industries Ltd. (Japan). DIP was made to couple with IAMS produced by CANON-ANELVA Corporation. The stock solutions were prepared separately by dissolving DMAA, TMAO, and AsE into methanol, and the working solutions with concentration of 0.01 mg/mL were prepared by dilution with methanol. Prepared sample reagents (1 μL) were taken into the sample tube and put into a thermostat (65 °C) for 10 min to remove methanol. Then, the sample tube was put into sample holder of DIP, and the DIP was inserted into the ionization room (IR) of IAMS. The temperature of sample tube increased to 400 °C in 1 min, and the sample were heated and gasified. After the gaseous sample attaching lithium ions, it was detected by a quadrupole mass spectrometer (QMS). QMS was operated in scan mode for 5–410 a.m.u.

The mass spectra of organoarsenic compounds detected by DIP-IAMS were shown in Figure 1. The molecule ion peaks of $DMAALi^+$, $TMAOLi^+$, and $AsELi^+$ were detected, which were m/z 145, 143, and 217, respectively. In addition, the peaks, m/z 25, 35, 39, and 65 were also observed in Figures 1a and 1b. For IAMS, nitrogen is used as the carrier gas, so N_2Li^+ (m/z 35) was highly detected. Concurrently, lithium ions react to water easily, the ever-present water in nitrogen carrier gas was observed as the peaks of H_2OLi^+ (m/z 25). These peaks were similar to the previous studies reported by Fujii et al. Moreover, methanol was used as solvent, and acetone was sometimes used to clean ion attachment section in this study, so the peaks

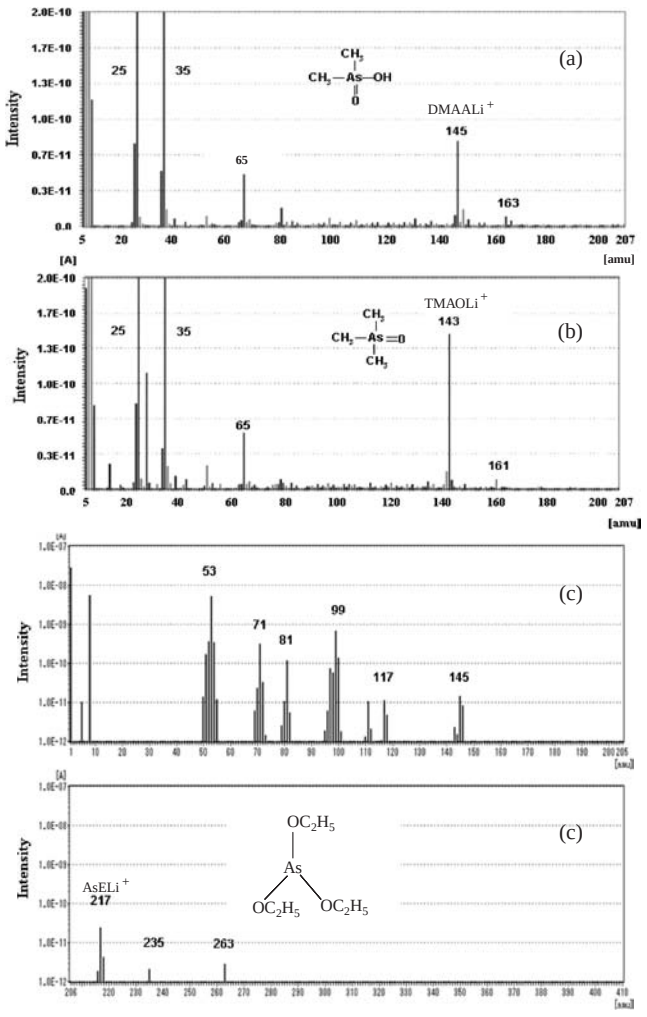

Figure 1. Mass spectra of three organoarsenic compounds: (a) DMAA, (b) TMAO, and (c) AsE by IAMS. 0.01 mg/mL × 1 μL of each compound was introduced.

of m/z 39 and 65 were derived from methanol and acetone. The peaks that presented water and nitrogen adduct to organoarsenic compounds were also observed, for example, the peak of $(DMAA + H_2O)Li^+$ (m/z 163), $(TMAO + H_2O)Li^+$ (m/z 161), $(AsE + H_2O)Li^+$ (m/z 235), and $(AsE + H_2O + N_2)Li^+$ (m/z 263), although the mechanism of some peaks' production was uncertain. The detection limits of DMAA, TMAO, and AsE were 0.35, 0.15, and 1.5 ng (S/N = 3), respectively.

For AsE, the mass spectrum that deducted the background was shown in Figure 1c, and some peaks were detected during m/z 50 and 150. These peaks were due to the ethanol, which derived from the reaction of AsE to H_2O. For example, the peaks of m/z 53, 99, and 145 maybe $EtOHLi^+$, $(2EtOH)Li^+$, and $(3EtOH)Li^+$, respectively. Therefore, the detection limit of AsE was higher than those of DMAA and TMAO. The other peaks of m/z 71, 81, and 117 were also observed and considered as $(EtOH + H_2O)Li^+$, $(EtOH + N_2)Li^+$, and $(2EtOH + H_2O)Li^+$.

From the results mentioned above, three organoarsenic compounds can be detected directly, and the direct detection of other organoarsenic compounds such as monomethylarsonic acid (MMAA), AB, and arsenosugars are also possible. Moreover, with the advantage of IAMS, the direct detection of mixture would be also possible. Therefore, the use of DIP-IAMS will help to analyze organoarsenic compounds or other organometallic compounds in biochemical and environmental samples simply and quickly. It was considered that DIP-IAMS should be paid more attention and developed into a new method that can do well in the chemical speciation of metallomics studies. The future application of DIP-IAMS in arsenic compounds' chemical speciation in organism is in the development.

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