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# Speciation of trimethyllead and triethyllead by in-tube solid phase microextraction high-performance liquid chromatography electrospray ionization mass spectrometry

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An analytical method has been developed for the determination of the trimethyl- (TML) and triethyllead (TEL) species in aqueous samples. In-tube solid phase microextraction (SPME) and high-performance liquid chromatography (HPLC) are coupled to a quadrupole mass spectrometer (MS) using electrospray (ES) as an ionization interface. Optimization of the instrumental parameters is described, including the evaluation of three commercial GC capillaries for the in-tube SPME experiments. The elemental ($^{208}Pb^{+}$) and molecular forms TML and TEL (*m/z* 253 and 295, respectively) were monitored simultaneously to provide complete speciation information. Results from the in-tube SPME-HPLC-ESMS experiments indicate that complete separation and detection of TML and TEL can be achieved in less than 5 min. Precision is greater than 5% and estimated limits of detection are 11.3 and 12.6 ng ml$^{-1}$, respectively, for TML and TEL at a solution flow rate of 450 μl min$^{-1}$.

## Introduction

Lead is one of the most common and important trace metals whose general toxic properties have been know since the early 1970s.[1] The massive use of organolead compounds in fuel as antiknock agents and the use of inorganic lead in battery production have caused a dramatic increase in the presence of these compounds in the environment. The toxicity of the tetraalkyllead compounds used in fuel is well known; however, the stability of these compounds in an aqueous environment is very low and they are often degraded into ionic alkyllead compounds. The toxic effects are maximal for the mono-positive cations, *i.e.*, the species derived by loss of one organic group from the neutral, fully saturated organometallic, *viz.* $R_3Pb^{+}$.[1] In general, the alkyl metal analogues are more toxic than aryl metals. The presence of these water soluble, relatively stable ionic species is very common in environmental samples. As a result there is a significant interest in developing a greater understanding of the origins, pathways, toxicity and biological effects of organolead in the environment. Without precise analytical methods capable of determining these species at trace levels, however, it is difficult to properly identify the environmental pathways of organolead compounds and make accurate risk assessments.

Over the last decade speciation analysis has become one of the fastest progressing techniques of modern instrumental elemental analysis. Speciation analysis focuses on the determination of specific chemical forms of a given element in a sample. In general, speciation measurements are performed using a high-performance separation technique that is coupled to an element selective (atomic spectroscopy) detector for the separation and detection of different species.[2] For volatile species (*e.g.*, organometallic species) a common approach is to couple gas chromatography (separation) with MIP-AES[3] or electrospray ionization (ES) MS[4] (detection). Commercial GC-EIS-MS systems can provide direct information on the molecular form of lead, although they usually lack the sensitivity required for trace or ultra-trace measurements. Although the application of atomic spectroscopic detection partially resolves this problem by providing sensitive element specific information, only indirect inference on the form of the element (speciation) can be made from the relative retention time of the analyte compounds. Perhaps a more problematic feature is that derivatization (alkylation) reactions are typically required for the analysis of ionic alkyllead compounds by GC-based speciation techniques. These are often complicated processes that require a great deal of time and reagent. In addition, the thermal stability of the non-ionic alkyllead compounds produced is sometimes low and, therefore, GC separation can be problematic. Detection of tetraalkyllead by HPLC-ICP-MS has provided detection limits of 5 pg for TML and TEL as $^{208}Pb^{+}$.[5] Although fairly sensitive, and used as an alternative to GC methods, this technique provides only indirect information on the form of Pb. A logical progression is to develop techniques capable of measuring the ionic organolead compounds directly in aqueous samples.

Electrospray mass spectrometry (ESMS) is one method that has demonstrated great potential for the direct determination of inorganic and organometallic complexes.[6–8] In ESMS, solution phase ions can be transferred to the gas phase from charged droplets for sensitive MS detection without extensive modification of their form. As such, ESMS has already been used successfully to determine a number of Pb species including the aqueous metal ion[9–13] and various metal–ligand complexes involving Pb.[14,15] Recently, Mester and Pawliszyn[16] have demonstrated that ESMS could also be used to determine trimethyllead (TML) and triethyllead (TEL) species.

Efficient sample preparation and preconcentration is an essential part of analytical methods used for the determination of species at trace levels in 'real samples'. Solid phase microextraction (SPME) techniques have already demonstrated a great proficiency for the selective extraction of a number of volatile organic and organometallic compounds.[17–24] The general theory and advantages of SPME are well known:[25] it is fast, solvent free and can readily be integrated into sampling–extraction–sample introduction systems. The use of SPME as an on-line sample clean-up and preconcentration technique, or use of in-tube SPME in which the extraction phase coats the inside of an open tube through which the sample is passed, is a logical extension for speciation analysis. Eisert and Pawliszyn[26] have already described the theory of in-tube SPME and a number of researchers have used it on line with ESMS.[16,27,28] In particular, Mester and Pawliszyn have successfully used it as part of the sample

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introduction system in the determination of organolead species.[16]

In this paper we describe an analytical system that integrates the selective extraction of in-tube SPME with reversed-phase HPLC-ESMS for the sensitive, direct determination of trialkyllead species in aqueous solutions. As such, the present research extends previous work[16] with direct application to real samples. Special attention is given to the optimization of instrumental parameters of ESMS for the detection of TML and TEL and the proper selection of the in-tube SPME capillary. Analytical figures of merit including analysis time, precision and limits of detection will also be discussed.

## Experimental

### Instrumentation

A Hewlett Packard 1100 HPLC system coupled to a Hewlett Packard 1100MSD detector *via* pneumatically assisted electrospray was used for all measurements. A schematic of the electrospray nebulizer/mass spectrometer is shown in Fig. 1. The separation column was a $C_{18}$ guard-column (Supelco, Bellfonte, PA). Sample was introduced onto the column either by liquid injection (5 μl) or using the on-line in-tube SPME. All electrospray mass spectrometry optimisation studies were performed using SCAN MS data collection ($m/z = 50$–600). Data acquired using the integrated in-tube SPME-HPLC-ESMS system were acquired using the selective ion data collection mode. All peaks were evaluated by their height.

### Reagents

Triethyllead chloride and trimethyllead chloride reagents were purchased from Alfa Aesar Chemical Company (Ward Hill, MA, USA). Stock 1 mg ml$^{-1}$ organolead standard solutions were prepared separately by adding 10 mg of each compound to a pre-weighed 15 ml screw cap vial containing 10 ml of methanol. The vials were closed with a Mininter valve (Supelco, Bellfonte, PA). Working solutions were prepared by appropriate dilutions of the stock solution.

### Safety considerations

Organollead compounds are highly toxic and, therefore, should be handled only in a fume hood, using appropriate protective clothing. They should be stored in a tightly sealed container in a cool dry place.

## Results and discussion

### Electrospray mass spectrometric study of TML and TEL

**General optimisation.** Finding the optimum ESMS conditions is a critical parameter necessary for the sensitive, accurate determination of TML and TEL ionic complexes. In the current system, a pneumatically assisted electrospray source is mounted perpendicular to the MS sampling capillary for off-axis sampling (Fig. 1). Pneumatic nebulization, generating a fine spray of droplets that is relatively insensitive to sample composition and solution flow rate, is achieved through the use of a micro concentric nebulizer. Off-axis sampling also permits the use of normal HPLC flow rates (0.5–1 ml min$^{-1}$). One disadvantage of this source is that, because the configuration is fixed, it might not be as amenable to lower solution flow rates (*e.g.*, 2–10 μl min$^{-1}$). Given the current system, however, parameters such as the nebulizer gas pressure, drying gas flow rate, sampling capillary voltage and the fragmentor voltage are important optimization parameters and have been evaluated for both TML and TEL total ion currents. The general response of each is given in Fig. 2.

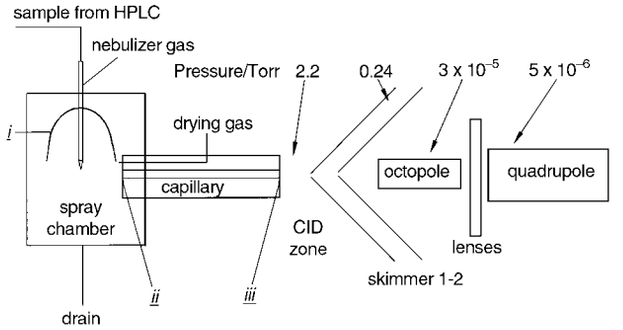


**Fig. 1** Schematic of the HP 1100MSD ESMS used for all experiments: *i* mesh electrode voltage = capillary voltage −500 V (same polarity); *ii* capillary voltage; *iii* fragmentor voltage.

The effect of the nebulizer gas pressure on the signal intensity for the measured compounds is shown in Fig. 2a. The nebulizer gas pressure affects the relative gas flow rate to the solution flow rate (450 μl min$^{-1}$) ratio and, thus, the nebulization efficiency. Higher gas flow rates can produce finer aerosols and, therefore, faster evaporation and consequently a greater rate of transfer of solution ions to the gas phase. Given the fixed location of the source, the efficient transfer of ions from the droplets to the gas phase close to the source can give rise to a dilution effect downstream of the source. This is based primarily on diffusion and space charge repulsion effects of ions within the spray which act to reduce the ion density in the gas volume that is sampled efficiently by the MS. Lower gas pressures result in the production of larger droplets and, therefore, a longer time for evaporation and slower transfer rates. A gas pressure of 40 psi, although a bit high, is efficient and provides a good compromise for each species.

The drying gas which flows counter-current from the sampling capillary (Fig. 1) is used to promote the efficient drying of droplets produced by the nebulizer in addition to minimizing the entrainment of neutral species. A low drying gas flow rate decreases the signal intensity through inefficient evaporation in addition to possible adduct formation in the low pressure region of the MS. The effect of the drying gas flow rate on the signal intensities for TML and TEL is shown in Fig. 2b.

The capillary voltage is applied to the entrance of the capillary that connects the spray chamber with the first vacuum stage (Fig. 1). The effect of the capillary voltage on the signal intensities for the TML and TEL ionic species is shown in Fig. 2c. The capillary acts as a counter electrode for the grounded spray chamber and nebulizer needle. The polarity of the capillary is, therefore, always opposite to the polarity of the ions analyzed. The optimum voltage is dependent on the charged aerosol characteristics, ions generated and the geometric parameters of the spray chamber. The optimum capillary voltage for the analysis of TML and TEL is between −2200 and −2600 V.

The effect of the fragmentor voltage on the total ion current for TML and TEL is depicted in Fig. 2d. The fragmentor voltage is applied at the exit end of the capillary (see Fig. 1). The applied voltage influences the fragmentation of the compounds and the transmission of ions. The optimum fragmentor voltage for the organolead compounds was between 60 and 70 V.

**The selection of fragmentor voltage.** Although Fig. 2d indicates that the maximum intensity for TML and TEL occurs at a fragmentor voltage between 60–70 V, other Pb ions generated from the fragmentation of these species can also be present. An example of this is given by the mass spectra acquired from 1 ppm solutions of the TML (Fig. 3a) and TEL (Fig. 3b) ionic species measured at 80 and 100 V fragmentation voltages, respectively. The masses in Fig. 3a and b are identified in Table 1. The fragmentation of trimethyllead and triethyllead was described in our earlier work.[16] In general, higher

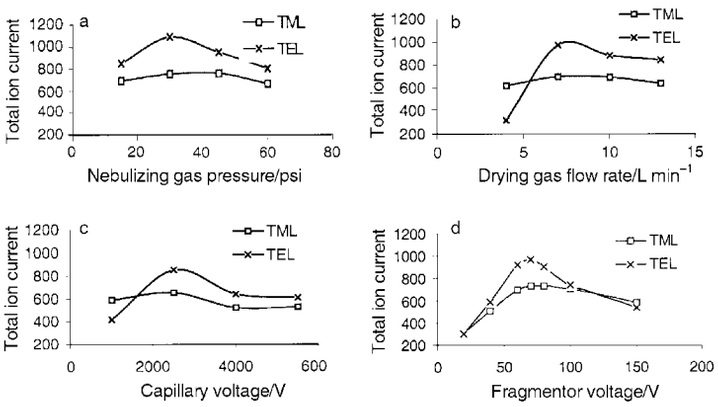


**Fig. 2** Effect of (a) nebulizer gas pressure; (b) drying gas flow rate; (c) capillary voltage; and (d) fragmentor voltage on the signal intensity of 1 ppm (by weight Pb) TML and TEL sample solutions.



fragmentation voltages result in higher fragmentation rates. High fragmentation voltages led to total decomposition of the organolead species into elemental lead. In some cases the isotopic ratios, shown in Fig. 3, indicate significant deviation from that predicted by the isotopes present. This may be due in part to the very fast scan rates and the transient nature of the sample introduction. As well, the exact isotopic ratio measurement of lead is greatly complicated by the presence of isobaric $PbH^+$ ions formed as residuals of the CID solvent/charge stripping conditions employed.[29,31]

The variation in the intensity of the TML and TEL parent ions and their respective fragmentation products (Table 1) generated using different fragmentation voltages is shown in Fig. 4a and b. The *y*-axis shows the relative intensity (%) of the different peaks, normalized at each fragmentation voltage for the most intensive ion. The effect of the fragmentation voltages on the mass peak distribution is clearly seen. The molecular ions dominate the response at lower applied voltages whereas the percentage of the molecular ions decreases and the elemental lead peak increases at higher applied voltages. Between the two "extreme" voltages can be seen an "optimum" distribution of the intermediate fragments. For analytical practice the most important question is how to choose the most intense peak for quantification in the selective ion mode (SIM). The absolute intensities of the mass peaks using different fragmentation conditions are shown in Fig. 5a and b. In the case of trimethyllead, the maximum intensity of the *m/z* 208, 223, 253 ions at the appropriate fragmentor voltages is practically the same. For quantification it should be possible to use all of these masses and achieve similar sensitivity. These results suggest that the simultaneous monitoring of the elemental and molecular forms of TML can be achieved with good sensitivity. The results for triethyllead show a different distribution. The most intensive ion is the *m/z* 295 at a 60 V fragmentation potential. The maximum intensity of elemental lead (*m/z* 208) is about 30% of the maximum intensity of the molecular ion. As such, both atomic and molecular forms can be monitored; however, the intensity of the elemental lead ion will be lower than the molecular TEL ion. For all subsequent speciation analysis, the atomic and molecular forms were monitored.

**Table 1** MS peak identification table for TML and TEL

| Trimethyllead | *m/z* | Triethyllead | *m/z* |
|---|---|---|---|
| $[Pb]^+$ | 208 | $[Pb]^+$ | 208 |
| $[Pb\text{-}(CH_3)\ ]^+$ | 223 | $[Pb\text{-}(CH_2CH_3)]^+$ | 237 |
| $[Pb\text{-}(CH_3)_2]^+$ | 238 | $[Pb\text{-}(CH_2CH_3)_2]^+$ | 266 |
| $[Pb\text{-}(CH_3)_3]^{+a}$ | 253 | $[Pb\text{-}(CH_2CH_3)_3]^{+a}$ | 295 |

[a]Parent molecular ion.

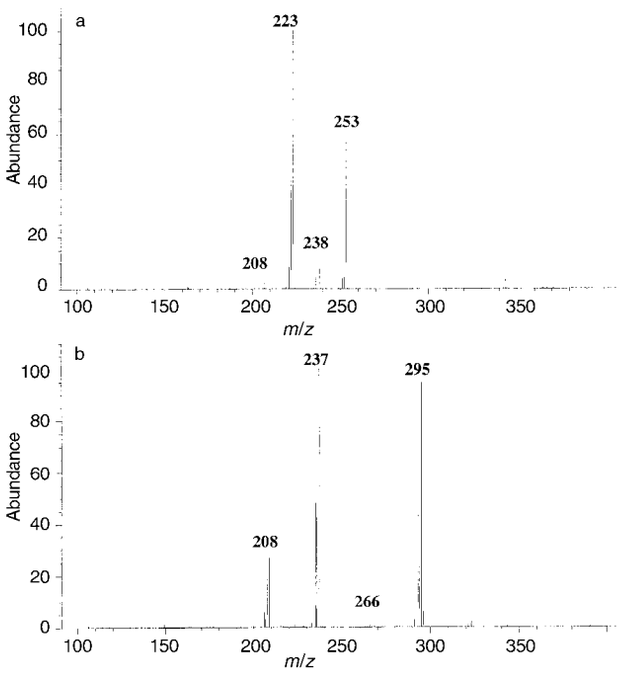


**Fig. 3** Mass spectrum of (a) TML and (b) TEL each 1 ppm (by weight Pb) acquired using 80 and 100 V fragmetor voltages, respectively. The figure demonstrates the different fragmentation products generated from the parent species as listed in Table 1.

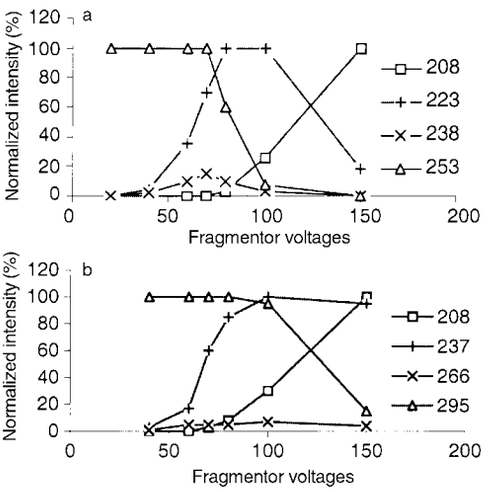


**Fig. 4** Effect of the fragmentor voltage on the percentage distribution of fragment ions (Table 1) generated from 1 ppm (by weight): (a) TML and (b) TEL signals.

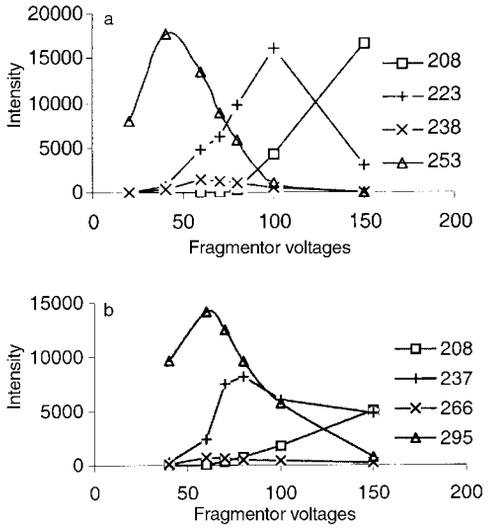


**Fig. 5** Effect of the fragmentor voltage on the raw signal intensity distribution of fragment ions (Table 1) generated from 1 ppm (by weight): (a) TML and (b) TEL signals.

### Coupling in-tube SPME to the speciation system

As stated above, in-tube SPME is essentially an open tube capillary coated on the inside with a suitable extraction polymer, connected to an HPLC system in place of the sample introduction loop. One of the main advantages of an in-tube extraction system is simple matrix separation. The polarity based extraction should efficiently separate target compounds from other small ionic constituents such as chloride, phosphate. Using an auto-injector with the 6 port valve in the "load" position, the capillary is washed several times with the sample solution, by applying "draw from sample–eject into the sample" extraction cycles. The cycles are repeated a number of times until an equilibrium is reached between the sample concentration and the concentration in the extracting phase. After the extraction step the valve is switched to the "inject" position and the mobile phase passes through the extraction capillary and into the HPLC column towards the ESMS detector. In this work the sample was desorbed from the capillary by the mobile phase. Fig. 6 shows the schematics of the in-tube solid phase microextraction system.

For the extraction, three polar GC capillary columns were tested: Supel-Q-Plot a porous divinylbenzene polymer coating, OmegaWax 250 a bonded poly(ethylene glycol) coating and Nukol a poly(ethylene glycol) modified with nitroterephthalic acid coating. A comparison of the efficiency of the three capillaries for the extraction of TML and TEL is shown in Fig. 7. The measurements were carried out using relatively long extraction times (15 extraction cycles) to ensure equilibrium.

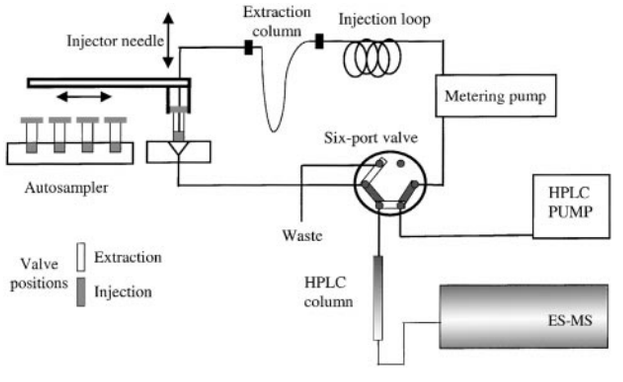


**Fig. 6** Schematics of the in-tube SPME-reversed-phase HPLC-ESMS system.

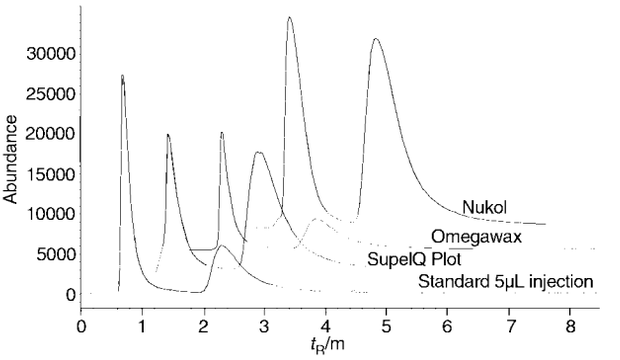


**Fig. 7** Comparison of three polar GC capillaries for TML and TEL extraction. All of the analyses were performed using the parameters described in Table 2. The solution concentrations are 1 ppm (by weight Pb) of TML and TEL.

For the SupelQ Plott and Omegawax capillaries the extractions are based on hydrophobic interactions between the compound, the mobile phase and the capillary coating. For the Nukol capillary, the interaction is based upon a light cation-exchange effect due to the presence of carboxylic functional groups in the modification agent. Because of this, the best results were obtained from the Nukol column. Optimization of the extraction conditions for TML and TEL using the Nukol capillary resulted in a preconcentration factor between ~2.3–5.9 for the two species. The optimum parameters for the extraction are summarized in the general method description in Table 2.

### Chromatography

The separation of trimethyllead and triethyllead was performed using a reversed-phase ($C_{18}$) precolumn. The polarity of the trimethylated and -ethylated species is sufficiently different to carry out conventional reversed-phase separations. Methanol was the non-polar component in the eluent system, and its composition was varied between 1–12% v/v with water to optimize the separation of the TML and TEL species. Results from separations performed using 2, 8 and 12% v/v methanol is given by the respective chromatograms shown in Fig. 8. The use of a 12% v/v methanol composition provided a fast separation with sufficient resolution (complete baseline separation was obtained). The method was optimized for trialkyllead species; however, some samples could contain also saturated

**Table 2** Instrumental parameters used for the in-tube SPME-HPLC-ESMS determination of TML and TEL

| | |
|---|---|
| *In-tube SPME—* | |
| GC capillary | Nukol 60 cm × 0.5 mm × 0.5 μm |
| Conditioning program | Draw 50 μl methanol into the capillary<br>Eject 50 μl methanol from the capillary |
| Extraction program | Draw 50 μl sample into the capillary<br>Eject 50 μl sample from the capillary |
| Number of extraction cycle | 15 |
| *HPLC—* | |
| Column | SUPELCO C-18 Nucleosil guard column<br>20 × 4.6 mm id, 3 μm particle size |
| Mobile phase | 0.1% TFA + 12% methanol |
| Flow rate | 0.45 ml $min^{-1}$ |
| *Electrospray/Mass spectrometer—* | |
| Ionization mode | Positive |
| Capillary voltage | 2500 V |
| Nebulizer gas pressure | 40 psi |
| Drying gas flow rate | 10 l $min^{-1}$ |
| Fragmentor voltage | $m/z$ = 208, fragmentor = 150 V<br>$m/z$ = 253, 295 fragmentor = 60 V |

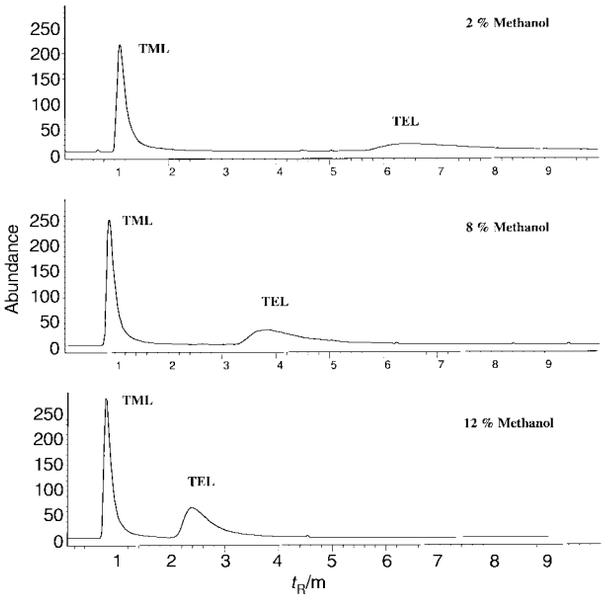


**Fig. 8** Effect of the methanol (% v/v) composition in the mobile phase eluent on the retention time of TME and TEL (1 ppm) based upon 5 µl liquid sample injections.

tetraalkyllead species. The tetraalkyl lead compounds are less polar than the trialkyls and in the reversed-phase separation environment would therefore be eluted significantly later than the trialkyl species and not affect the determination of the trialkyl species.

### Method performance

The optimized conditions for the in-tube SPME-HPLC-ESMS system are summarized in Table 2. The TML and TEL calibration was linear in the range 50–30,000 ng ml$^{-1}$. The analytical characteristics of the system are presented in Table 3. The RSD of five replicates was calculated at the 200 ng ml$^{-1}$ concentration level of TML and TEL, and the detection limit was calculated based on the 3σ criterion. The retention times are sufficiently short to allow the rapid determination of both components. The proposed system was applied to drinking water. Upon analysis it was found that no organolead was found in the samples within the detection range of the system. The samples were spiked with TML and TEL; the average results of three parallel measurements and the recovery data are shown in Table 4. Fig. 9 shows a typical chromatogram of TML and TEL extracted from drinking water.

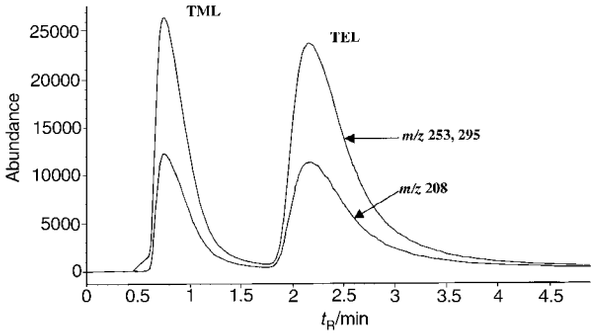


**Fig. 9** Chromatogram of TML and TEL obtained by in-tube SPME-HPLC-ESMS. The concentration of each compound is 50 ng ml$^{-1}$. Both chromatograms were recorded simultaneously by monitoring the molecular masses (*m/z* 253, 295) of TML and TEL and in parallel the elemental lead mass (*m/z* 208).

## Conclusions

This study demonstrates the separation and determination of triethyl- and trimethyllead compounds by in-tube SPME-HPLC-ESMS. In-tube SPME is a simple and integrated tool for sample extraction, clean-up, preconcentration and sample introduction. The separation is simple, fast and inexpensive, employing only a $C_{18}$ guard column. The use of electrospray mass spectrometry detection allowed us to simultaneously obtain information from both the elemental and molecular forms of the lead. A very important advantage of ESMS is that it can combine both element specific and direct molecular structure information for the detection of TML and TEL species. The current detection limits reported using in-tube SMPE-ESMS are 11.3 and 12.6 ng ml$^{-1}$ for TML and TEL, respectively. These detection limits are comparable to those currently reported using HPLC-ICP-MS (5 pg).[5] It is anticipated that a further reduction in detection limits using the current system can be achieved through better optimisation of the detection system, in particular, by moving to lower solution flow rates. Regardless, in-tube HPLC-ESMS represents an integrated approach capable of the preconcentration and sensitive direct determination of environmental species.

## Acknowledgements

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**Table 3** Retention times, detection limits and relative standard deviations of the in-tube SPME-HPLC-ESMS method

| Lead species | Retention time/min | Detection limit/ng ml$^{-1}$ [a] | RSD[b] (%) |
|---|---|---|---|
| TML | 0.78 | 11.3 | 3.73 |
| TEL | 2.36 | 12.6 | 4.12 |

[a]Calculated for lead. [b]$n = 5$, using 200 ng ml$^{-1}$ TML and TEL standard solution.

**Table 4** Spiking study of tap water with TML and TEL

| Water sample[a] | Spiked TML/ ng ml$^{-1}$ | Spiked TEL/ ng ml$^{-1}$ | Found TML/ ng ml$^{-1}$ | Found TEL/ ng ml$^{-1}$ | Recovery TML (%) | Recovery TEL (%) |
|---|---|---|---|---|---|---|
| N 1 | 200 | 200 | 221 | 205 | 111% | 103% |
| N 2 | 100 | 100 | 115 | 110 | 115% | 110% |
| N 3 | 50 | 50 | 60 | 63 | 120% | 126% |

[a]For the spiking test the same water sample was used.

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