Sample-extraction methods for ion-mobility spectrometry in water analysis

Sanna Holopainen, Marjaana Nousiainen, Osmo Anttalainen, Mika E.T. Sillanpää

The requirement to monitor the chemical quality of water has become one of the major issues in environmental analytics. Ion-mobility spectrometry (IMS), a fast, sensitive method traditionally used in security and military applications, is also suitable for environmental analysis and detection of organic pollutants from aqueous matrices, when combined with advantageous methods to isolate analytes from the water phase.

This article reviews the current literature on the sample-extraction methods most feasible for aqueous samples prior to ion-mobility analysis, and highlights their principles and trends in IMS applications. These partition-based methods include solid-phase microextraction, stir-bar sorptive extraction, single-drop microextraction, hollow-fiber liquid-phase microextraction, pervaporation-membrane extraction and paper spray.

We also discuss comparisons of method characteristics and relative performance, and conclude that IMS is a potential method for both on-line and on-site determination of organic pollutants in aqueous matrices.

Keywords: Hollow-fiber liquid-phase microextraction (HF-LPME); Ion-mobility spectrometry (IMS); Sample extraction; Sample pretreatment; Single-drop microextraction (SDME); Solid-phase microextraction (SPME); Stir-bar sorptive extraction (SBSE); Monitoring; Water analysis; Water quality

Abbreviations: AIMS, Aspiration ion-mobility spectrometry; BTEX, Benzene, toluene, ethyl benzene, xylene; CAR/PDMS, Carboxen/polydimethylsiloxane; CD, Corona discharge; DI, Direct immersion; DLR, Dynamic linear range; DMS, Differential mobility spectrometry; EPA, US Environmental Protection Agency; ESI, Electrospray ionization; FAIMS, Field asymmetric waveform ion-mobility spectrometry; GC, Gas chromatography; HF-LLLME, Hollow-fiber liquid-liquid-liquid microextraction; HF-LPME, Hollow-fiber liquid-phase microextraction; [Hmim][NTf_2], 1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonyl) imide; HPLC, High-performance liquid chromatography; HS, Headspace; HSSE, Headspace sorptive extraction; IL, Ionic liquid; IMMS, Ion-mobility mass spectrometry; IMS, Ion-mobility spectrometry; IMS-MS, Ion-mobility spectrometry-mass spectrometry; LC, Liquid chromatography; LLLME, Liquid-liquid-liquid microextraction; LOD, Limit of detection; LPME, Liquid-phase microextraction; MCC, Multicapillary column; ME-IMS, Membrane-extraction ion-mobility spectrometry; MMLLE, Microporous membrane liquid-liquid extraction; MQL, Method-quantification limit; MS, Mass spectrometry; MTBE, Methyl *tert*-butyl ether; [Omim][PF_6], 1-octyl-3-methylimidazolium hexafluorophosphate; PA, Polyacrylate; PAH, Polyaromatic hydrocarbon; PCB, Polychlorinated biphenyl; PCE, Tetrachloroethylene; PDMS, Polydimethylsiloxane; PME, Polymeric membrane extraction; PP, Polypropylene; PPy-DS, Polypyrrole-dodecylsulfate; PV, Pervaporation; RDX, 1,3,5-trinitro-1,3,5-triazine; RSD, Relative standard deviation; RTGC, Room-temperature gas chromatography; SBSE, Stir-bar sorptive extraction; SDME, Single-drop microextraction; SLM, Supported liquid membrane; SPME, Solid-phase microextraction; 2,4,6-TCA, 2,4,6-trichloroanisol; 1,2,4-TCB, 1,2,4-trichlorobenzene; TCE, Trichloroethylene; TD, Thermal desorption; TFME, Thin-film microextraction; TOF, Time-of-flight; TNT, Trinitrotoluene; TWA, Time-weighted average; UV, Ultraviolet ionization; UV-Vis, Ultraviolet-visible light detector; VOC, Volatile organic compound; WFD, Water Framework Directive of European Union; WHO, World Health Organization

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0165-9936/$ - see front matter © 2012 Elsevier Ltd. All rights reserved. doi:http://dx.doi.org/10.1016/j.trac.2012.03.014

1. Introduction

Monitoring the chemical quality of water is required by environmental legislation [e.g., the Water Framework Directive (WFD) of the European Union], and advised by several regulatory guidelines and protocols throughout the world [e.g., World Health Organization (WHO) and US Environmental Protection Agency (EPA)] [1]. For this purpose, the development of fast, straightforward sample-preparation and detection techniques is one of the key issues in environmental water analysis [2,3]. Several review articles were published recently about sample-preparation techniques suitable for quantifying environmental pollutants [4–12]. Recent method development has been based on the principles of green chemistry (e.g., the possibility of automation and miniaturization, preference for analytical methods at ambient pressure and temperature, and direct analysis) [13,14]. Importantly, also, microextraction techniques that are solventless, or with virtually no solvent, have been studied [15].

In modern environmental analysis, fast, sensitive detection techniques [e.g., ion-mobility spectrometry (IMS)] are favored. IMS is based on determining analyte mobilities in the ambient gas phase and can analyze organic and inorganic species in trace concentrations [16]. Traditionally, IMS has been used in detecting explosives, chemical-warfare agents (CWAs) and illicit drugs [17,18]. IMS has also been successfully applied to processes where the purity or the safety of process is being monitored [e.g., quality control in the pharmaceutical and food industries, plants and person safety, and human health (breath analysis)] [19,20]. Various characteristics make IMS feasible for environmental applications, since it can operate on-site, real-time analysis in a full range of environmental conditions [21] and can determine pollutants from different kinds of matrices [22]. IMS also combines low technical costs with high-speed data acquisition [21].

This article presents the potential of IMS in determining harmful chemicals in water and reviews the current literature of sample-extraction methods suitable for water samples and IMS. Extraction methods considered are solid-phase microextraction (SPME), stir-bar sorptive extraction (SBSE), single-drop microextraction (SDME) and pervaporation ME (PVME) – as potential methods for IMS – hollow-fiber liquid-phase microextraction (HF-LPME) and paper spray. Although the latter two methods are not described for the environmental aqueous samples in combination with IMS, they also have potential in this field. This means that HF-LPME and PVME are in future useful methods also in environmental analysis.

We discuss the principles of IMS and its applications with partition-based methods. Also, we discuss comparison of method characteristics. Table 1 summarizes these methods and their IMS applications for the determination of aqueous environmental samples.

2. Ion-mobility spectrometry

IMS is a straightforward, low-cost analytical method, which provides fast responses to analytes and low levels of detection (ppb). IMS performance has often been compared to the performance of mass spectrometry (MS) [21], and, although IMS is less selective, it is less expensive and easier to operate than MS. IMS has generally not been used to identify unknown chemicals. Rather, it is suitable for the determination of hazardous chemicals in processes where the composition is known. The sensitivity of IMS is similar to the sensitivity of flame-ionization detectors in gas chromatography (GC) and better than that of UV-Vis adsorption detectors in liquid chromatography (LC) [23].

Ion-mobility measurements are based on the drift velocities of ions in the electric field at ambient pressure. A conventional sort of IMS is the time-of-flight (TOF) design, which has a similar principle to MS-TOF with the exception of operating at atmospheric pressure, and it comprises reaction section, ion shutter, drift tube, and detector (Fig. 2).

Prior to IMS analysis, the sample needs to be delivered to the ionization region by direct sample introduction (gaseous samples) or after pretreatment of the sample (aqueous and solid samples). Different kinds of sample-introduction units and sample-preparation methods suitable for gaseous, liquid, and solid samples have been examined for IMS [22]. Sample-introduction units for IMS are direct inlets, membrane-extraction inlets, thermal desorption (TD) units, thermal pyrolysis units, GC, including multicapillary columns (MCC), and LC. The known methods for sample preparation for IMS include SPME and SBSE [16,22]. The development of sample-preparation methods makes IMS more feasible for real-time analysis from various environmental matrices.

Ionization of neutral molecules in IMS can be performed by chemical ionization (secondary ionization) where reactant ions are hydrated protons, $H^+(H_2O)_n$ in the positive mode and hydrated O_2^- in the negative mode ($O_2^-(H_2O)_n$). These primary ions can be formed with the help of β-particles or α-particles emitted from radioactive sources (^{63}Ni, ^{3}H, ^{241}Am). The product ions formed are monomer and dimer ions (in positive-mode $MH^+(H_2O)_n$ and $M_2H^+(H_2O)_n$, respectively) (Fig. 3), and their intensity is concentration dependent. Molecules can also be ionized by corona discharge (CD), UV lamps (photoionization), electrospray ionization (ESI), surface ionization, laser ionization, and plasma ionization [16]. Because there are differences in the ion chemistry with different ionization sources {e.g. chemical ionization is governed by proton affinities and photoionization by ionization energies [16]}, the sensitivity of IMS analysis can be enhanced by selecting a proper ionization method.

Table 1. Ion-mobility spectrometry (IMS) studies of aqueous environmental samples, performed in water, unless otherwise stated

Method	Analyte	IMS mode	LOD	Extraction material	Other remarks	Ref.
HS-SPME	Se(IV)	CD-IMS	12 ng/mL	PPy		[38]
	MTBE	^{63}Ni-IMS	5 mg/mL	75 μm CAR/PDMS fiber		[39]
	MTBE	^{63}Ni-IMS	0.7 ng/mL	PPy-DS fiber		[40]
			4.9 ng/mL	PPy-DS fiber		
	Atrazine	CD-IMS	15 ng/mL	PPy-DS fiber		[42]
	Ametryn		10 ng/mL	PPy-DS fiber		
	Benzene	GC/^{63}Ni-DMS	1.19 μL/L	100 μm PDMS fiber		[41]
	Toluene		1.24 μL/L			[43]
	Ethylbenzene		0.07 μl/L			
	m-, *o*-, *p*-xylene		0.01 μL/L			[44]
	BTEX, naphthalene	MCC/UV-IMS	<1 mg/L	100 μm PDMS fiber		
	Tetrachloroethene		<1 mg/L	85 μm PA fiber		
	1,2,4-TCB	GC/DMS	<1 mg/L	85 μm PDMS fiber		
DI-SBSE	TNT	^{63}Ni-IMS	0.1 ng/mL	PDMS sorbent		[48]
	RDX		1.5 ng/mL			
IL-HS-SDME	2,4,6-TCA	^{3}H-IMS	0.2 ng/L	IL = [Hmim][NTf_2]		[54]
	2,4,6-TCA	MCC/^{3}H-IMS	0.01 ng/L	IL = [Hmim][NTf_2]	Wine sample	[55]
	Bromodichloromethane	RTGC/^{3}H-IMS	0.13 ng/mL	IL = [Omim][PF_6]		[53]
	Bromoform		0.10 ng/mL			
	Chloroform		0.91 ng/mL			
	Dibromochloromethane		0.19 ng/mL			
HF-LPME	Clomipramine	CD-IMS	0.35 μg/L	PP hollow fiber with n-dodecane	Urine sample	[59]
(LLLME)	Trimipramine, desipramine	ESI-IMS	5 μg/L (MQL)	PP hollow fiber with n-dodecane	Urine sample	[60]
	Pentazocine	ESI-IMS	2 ng/mL	PP hollow fiber with n-octanol	Urine sample	[61]
Pervaporation membrane extraction	TCE	^{63}Ni-IMS	74 μg/L	Hollow PDMS membrane		[65,66]
	PCE		80 μg/L			
	Benzene	UV-DMS	10 mg/m^3	PDMS capillary		[67]
	MTBE	^{63}Ni-IMS	100 μg/L	Flat silicone membrane		[68]
		CD-IMS	100 μg/L			[69]
	MTBE	MCC/UV-IMS	20 mg/L	PDMS membrane extraction unit		
		MCC/^{63}Ni-IMS	1 μg/L			
Paper spray	Chlorpromazine	IMS	1.5 ng/μL		Urine sample	[71]

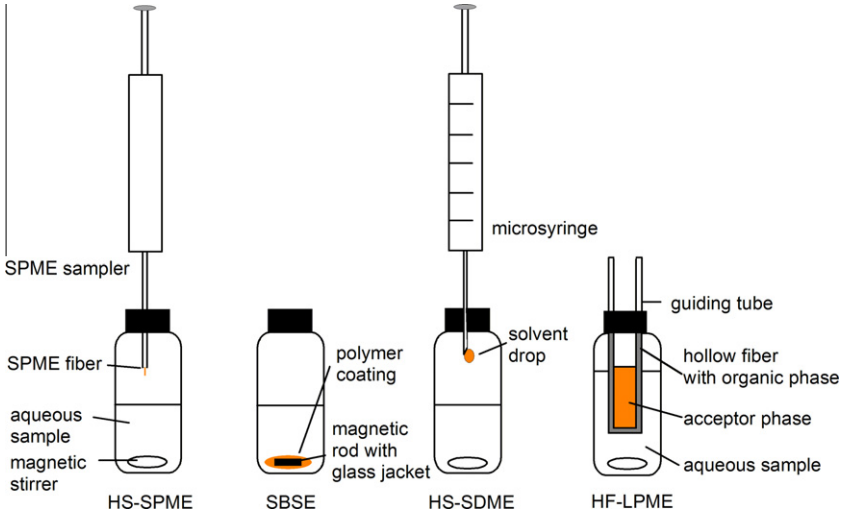

Figure 1. Extraction methods presented in this article.

In TOF-IMS, ions are transferred to the separation region in pulsed packets via a shutter grid. Sample ions are separated in the drift section in an electric field, typically 200–400 V/cm, and detected with a Faraday plate. Other methods for ion separation are differential mobility spectrometry (DMS) and field asymmetric

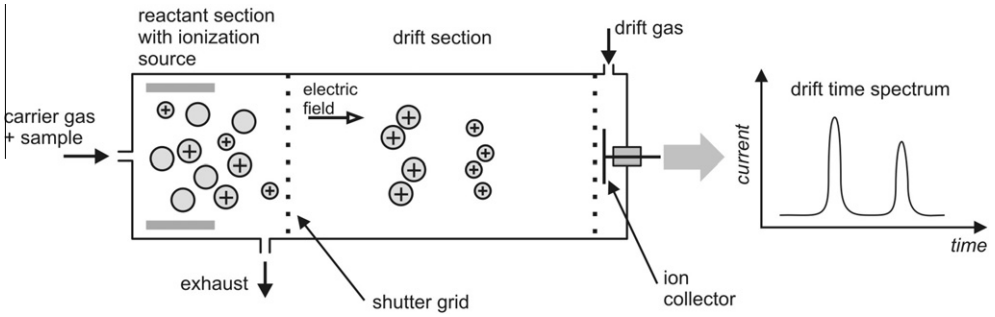

Figure 2. The principle of operation of time-of-flight ion-mobility spectrometry (IMS).

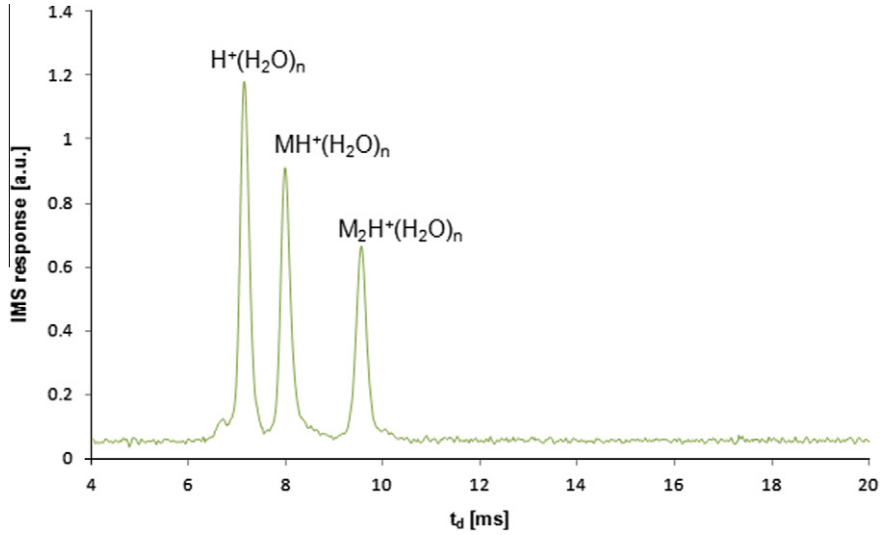

Figure 3. Ion-mobility spectrum of MTBE. The gas-phase concentration of the sample was 25 ppb.

waveform IMS (FAIMS), which work as ion-mobility filters with a variant electric field (>10 000 V/cm). The third type of analyzer, aspiration IMS (AIMS), is based on continuous measurement of ion dispersions, and it provides fast responses of mobility distributions instead of drift times [16].

Because ion separation occurs in milliseconds (ms), the total analysis time for one sample can be only a few minutes, including sampling, data acquisition and the recognition of sample. The sample recognition is based on drift times, and sample mobilities are comparable by reduced mobility coefficients (K_0), where drift properties (e.g., drift time, drift temperature, and electric field) have been taken into account. Drift velocities depend on not only the mass of ions, but also their structure, shape, and electrical properties [16]. As a consequence, ions with the same mass-to-charge ratio (isobars) can be separated with IMS.

The selectivity of IMS analysis can be enhanced by using proper pre-concentration methods [21], alternative reagent gases (dopants) [16,24] or coupled methods [16]. Coupled methods improve IMS performance, and bring synergistic benefits. For example, chromatographic separation coupled to IMS (GC-IMS or LC-IMS) improves the selectivity by eliminating possible interfering substances in ionization reactions during analysis [16]. IMS coupled with MS (IMS-MS or IMMS) with ESI is powerful tool for rapid analyses of complex mixtures in medicine and structural biology [16,25]. This combination is advantageous, because IMS offers the possibility for isomer separation, and MS provides valuable information about the mass identification of ions.

IMS is said to be more easily adaptive to real-time monitoring than other laboratory instruments [21], and it has been used to monitor various industrial processes. IMS has been successfully applied to quality control in the pharmaceutical, polymer, petroleum and food industries [19]. For example, IMS has been used in on-line monitoring of polymerization reactions, in which it provides information about the course of reactions, intermediates and end products without time-consuming HPLC separation [19].

Table 2. Fundamentals of sample-extraction methods considered [8,9,27–29]

Method	Analyte (donor)	Extracting phase (acceptor)	Equilibrium	Phenomena
HS-SPME	Liquid	Solid	Liquid-gas-solid	Sorption, partition
DI-SBSE	Liquid	Solid	Liquid-solid	Sorption, partition
IL-HS-SDME	Liquid	Liquid	Liquid-gas-liquid	Partition
HF-LPME (LLLPME)	Liquid	Liquid	Liquid-liquid-liquid	Partition
Pervaporation membrane extraction	Liquid	Gas	Liquid-solid-gas	Partition, diffusion, evaporation
Paper spray	Liquid	Solid	Liquid-solid	Partition

In the field of environmental analysis, IMS has been successfully applied to the monitoring of hazardous vapors in both outdoor and indoor air, and the detection of contaminants in aqueous media to prevent environmental accidents [19,20]. The development of sample-preparation methods makes IMS more feasible for on-line analysis of various environmental matrices.

3. Sample preparation

Sample preparation can be considered the most critical step in environmental water analysis because it is typically the primary source of errors and discrepancies between laboratories [9,26]. The sample-preparation process involves analyte isolation from the primary matrix, separation of analyte molecules from interfering compounds present in the sample, analyte transfer to a phase appropriate to the detector chosen, and enrichment of analytes. To avoid sample losses, methods that combine several sample-preparation steps (e.g., isolation and enrichment) are favorable [9].

The selection of the appropriate sample-preparation method depends on the physicochemical properties of the analyte (e.g., the octanol-water partitioning coefficient ($K_{o/w}$) gives an estimation for SPME and SBSE analysis of how well the solutes can be extracted). Furthermore, for headspace analysis, volatile analytes with high Henry's law constants are favored [27]. Typically, in extraction-based techniques, the extractant (acceptor) is in contact with the sample matrix (donor) and analytes are transported between phases. As exceptions, in HF-LPME and PV, the sample is separated from the acceptor-phase by the membrane. The thermodynamics of the extraction process are defined by extraction phase/sample-matrix distribution constant. Consequently, the analytes are extracted on the basis of their solubility into the extracting phase [8,27].

Table 2 illustrates different phenomena taking place using the chosen methods. When solid phase is used in the extraction (e.g., SPME and SBSE), both sorption and partition phenomena occur. The sorption phenomenon is governed by intermolecular forces (i.e. hydrogen bonds and other dipole-dipole interactions between the analyte and the solid extracting phase). By contrast, when only the liquid phase is present, the partition phenomenon is governed by the solubility between phases [8]. Furthermore, in PV, the transport of analytes can be described by three steps:

(1) analytes are partitioned from the liquid to the membrane;
(2) diffusion through the membrane according to Fick's first law; and,
(3) evaporation from the membrane to the gas phase [28].

In paper spray, the analytes are separated by the distribution between paper and solvent phase (paper chromatography) [29].

4. Sample-extraction methods applicable for IMS

In the following sub-sections, we describe sample-extraction methods suitable for aqueous matrices and their IMS applications. We summarize and compare their main characteristics in Table 3. These methods are feasible for different sample polarities, fast (in a time-scale of minutes) and may be automated.

4.1. Solid-phase microextraction

Solid-phase microextraction (SPME) is a solventless sample-preparation technique that has also been widely used for environmental analysis [30–32]. SPME is based on the sorption/desorption of analytes on chemically-modified silica fiber, typically made from polydimethylsiloxane (PDMS). PDMS suits non-polar analytes, and many other fiber-coating materials have been developed {e.g., polypyrrole (PPy), which makes it feasible to extract polar analytes} [30].

One advantage of the SPME method is to analyze polar and non-polar analytes both on-site and on-line from gaseous, aqueous, and solid matrices. Various configurations of SPME have been used in water analysis. A typical SPME-fiber assembly, headspace SPME (HS-SPME) (Fig. 1), is suitable for chemicals with a high Henry's law constant. In the case of less volatile compounds, it is possible to perform the extraction by immersing the fiber directly in the solution (DI-SPME).

Table 3. Comparison of sample-extraction methods applicable for ion-mobility spectrometry

Aspect compared	SPME	SBSE	IL-SDME	HF-LPME	Membrane extraction	Paper spray
Cost	Medium	Medium	Medium	Low	Low	Very low
Portability	Medium	Medium	Medium	Medium	Medium	High
Ease of use	Relatively easy	Easy	Relatively easy	Relatively easy	Easy	Very easy
Maintenance	Low	Low	Medium	Medium	Low	Very low
Speed	Medium	Medium	Medium	Medium	High	High
Sensitivity	High to medium	High	High	High	High	High to medium
Selectivity	High	Medium	Medium	High	Low	Low
Applicability for different samples	Broad	Limited	Broad	Limited	Broad	Broad
Possibility for on-line analysis and automation	High	Relatively high	Relatively high	Relatively high	High	Low

In-tube SPME obtains time-weighted average (TWA) concentrations of pollutants, and thin-film microextraction (TFME) with higher extraction efficiency has been applied to water sampling in the field [30].

SPME can be used for quantitative analysis at very low analyte concentrations. The advantage is that the method can be automated, and is therefore suitable for on-line analysis using an autosampler [32]. In addition, because sampling, extraction and concentration are integrated into the same procedure, the losses occurring during traditional sample-preparation processes can be avoided in SPME. However, SPME is suitable for only a limited range of analytes, because of the selection of commercially-available stationary phases [32]. A further disadvantage is that fiber materials are relatively costly and fragile [33].

SPME is an effective pre-separation technique for IMS because the analytes can be directly transferred from SPME fiber to the gas phase on the timescale of minutes. SPME has been successfully coupled to IMS in the detection of drugs, explosives, and explosive taggants, mainly from air, but also water [34–37].

The combination of SPME and IMS or differential mobility spectrometry (DMS) has been used for environmental water analyses in fewer studies [38–44].

In a recent study, SPME was utilized in a less common metal-ion determination with IMS analyses. HS-SPME was used in the determination of selenium(IV) from environmental surface water and human blood [38]. It was possible to derivatize selenious acid into a volatile organometallic compound, piaselenol, and determine it with ESI-IMS in the concentration range 20–320 ng/mL of water.

SPME coupled to IMS has also been utilized in the determination of the groundwater and surface-water contaminant, methyl *tert*-butyl ether (MTBE). This gasoline additive has been evaluated from the headspace of surface-water, groundwater and gasoline samples with different SPME fibers [39,40].

A recent study showed that commercially-available 75-μm carboxen/polydimethylsiloxane (CAR/PDMS) fiber is suitable for fast determination of MTBE in combination with ^{63}Ni-IMS. HS-SPME-IMS was found to be a straightforward method for measurements of surface-water and groundwater samples with MTBE concentrations greater than 5 mg/mL [39].

In another study, MTBE was evaluated from the headspace of water and gasoline with a new SPME-fiber material, electrochemically-synthesized dodecylsulfate-doped polypyrrole (PPy-DS). Two linear calibration curves were obtained for MTBE in the ranges 2–17 ng/mL and 10–70 ng/mL with the limits of detection (LODs) of 0.7 ng/mL and 4.9 ng/mL, respectively [40].

In analyses of BTEX and other aromatic hydrocarbons, SPME has been found to be a sensitive sample pre-separation method for both DMS and IMS [41,43].

SPME combined with a portable GC-DMS has been applied to on-site analysis of BTEX compounds from surface waters. The method was sensitive to the separation and the detection of benzene, toluene, ethylbenzene, and *m*-, *o*- and *p*-xylenes. The LODs for these compounds were in the range 0.01–1.19 μg/L [41].

In another study, UV-IMS with multicapillary-column (MCC) separation was found to be capable of detecting BTEX, naphthalene, chlorinated alkanes, and chlorinated benzenes from groundwater and surface water with LODs in the upper-μg/L range, also in field conditions. It was suggested that the MCC/UV-IMS method can be suitable for field measurements after environmental accidents or during remediation processes, where the concentration of contaminants studied can be in the range of mg/mL [43].

SPME-IMS has also been used in the determination of atrazine and ametryn from water and soil samples. HS-SPME-IMS obtained LODs comparable to other analytical methods (15 ng/mL and 10 ng/mL for atrazine and ametryn from water, respectively), and a linear calibration range.

CD-IMS could detect these herbicides in a few milliseconds, while it took 30–40 min for chromatographic separation with GC or LC [42].

An early study, which combined SPME and UV-DMS, was found to be feasible for the determination of 1,2,4-trichlorobenzene from surface waters. In this study, the performance of SPME-GC-DMS was compared to that of SPME-DMS. DMS coupled to GC separation obtained an LOD below 1 μg/dm^3, and the linear calibration range of SPME-DMS was 0.1–10 mg/dm^3. SPME coupled to GC-DMS was found to be sensitive enough for the screening of water samples in field conditions [44].

4.2. Stir-bar sorptive extraction

Stir-bar sorptive extraction (SBSE) is based on the sorptive extraction of analytes. Analytes are sorpted on a spinning glass-covered magnetic bar, which is coated with a thin layer of PDMS. SBSE is a dynamic variation of SPME, and the analytes are transferred to an analytical device by a TD unit. Because of the apolar character of the PDMS coating, SBSE is most suitable for non-polar and weakly polar analytes. In addition, in-house produced stir-bar coatings have been produced for the extraction of polar analytes [45,46].

Although SBSE and SPME are both based on the same principle, the stir-bar coating has a larger sorbent volume (24–100 μL) compared to SPME fiber (0.5 μL), and this enables the higher enrichment factor of SBSE. SBSE is therefore more sensitive, though it has longer extraction times than SPME [46].

Stir-bar sorptive sampling can be performed from liquid, as SPME in headspace (HSSE) or direct immersion (SBSE) mode (Fig. 1).

In environmental analyses, SBSE has been used to evaluate organic contaminants from different matrix types (e.g., water, soil, and aerosol) [45–47].

The combination of SBSE with IMS has been reported in only the trace analysis of explosives from water [48], although the method is also suitable for determining other aqueous pollutants.

This study developed an interface with the TD unit for SBSE-IMS analysis, and trinitrotoluene (TNT) and 1,3,5-trinitro-1,3,5-triazine (RDX) were detected from water samples with the LODs 0.1 ng/mL for TNT and 1.5 ng/mL for RDX. SBSE-IMS has potential for sensitive on-site detection of explosives that are difficult to determine using GC or HPLC.

4.3. Single-drop microextraction

With other LPME techniques, single-drop microextraction (SDME) has been utilized in the analysis of polar organic contaminants from aqueous samples [7,49,50]. SDME is virtually a ''no solvent'' extraction method, as it needs only a few μL of solvent. Usually, a 1–3 μL drop of solvent is suspended from a tip of a microsyringe needle and placed in the liquid sample phase (direct-immersion, DI-SDME) or above the headspace (HS-SDME) (Fig. 1). After the equilibrium time, the solvent is retracted back to the syringe with the extracted sample and subjected to further analysis [49,50].

The potential advantage of SDME is in-drop derivatization (i.e. adding derivatization or complexation reagent to an extractive drop provides more functionality) (''active'' SDME).

However, the method is not on average very accurate because of the instability of the solvent drop. To improve reproducibility of this extraction method, a fully automated autosampler system has been developed [49,50].

SDME is a fast, inexpensive method that does not in principle require any special equipment. The only consumable is the solvent, and, typically, water-immiscible solvents, (e.g., 1-octanol, toluene and acetonitrile) are used [49,50].

More environmentally friendly solvents are ionic liquids (ILs), and their major advantages are higher viscosity, which facilitates larger drop volumes, lower volatility, longer extraction times, and increased precision and accuracy in contrast to other organic solvents [51]. However, the non-volatile character of ILs makes them incompatible with direct coupling to analytical instruments, so special interfaces have already been developed [52].

IMS coupled to IL-SDME offers a rapid, simple way to analyze organic pollutants, and this combination has been used to evaluate environmental pollutants (e.g., halocompounds) from aqueous matrices [53–55]. IL 1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonyl) imide {[Hmim][NTf_2]} has been utilized as an SDME solvent with IMS in the determination of 2,4,6-trichloroanisole (2,4,6-TCA) that causes a musty odor in water and wine samples [54,55]. 2,4,6-TCA was directly extracted from water by IL-SDME, whereas wine samples were treated by solid-phase extraction (SPE) before IL-SDME. In this study, the LODs obtained were 0.2 ng/L and 0.66 ng/L from water and wine, respectively.

In another study, IL-SDME-IMS coupled to MCC separation was found to be a suitable method for direct analysis of 2,4,6-TCA from wine samples without any additional treatment of sample other than dilution. The method was capable of achieving an LOD of 0.01 ng/L, and the results obtained were comparable to those from other analytical methods (e.g., MS). [55] In both of these studies, LODs obtained indicated TCA detection was highly sensitive {i.e. well below the human-perception threshold for haloanisoles in drinking water and wines (4 ng/L and 10 ng/L, respectively)} [54,55].

IL-HS-SDME has also been coupled to room-temperature GC-IMS (RTGC-IMS) for direct determination of trihalomethanes from environmental water samples. In this study, an injection unit was designed for the direct transfer of IL-extracted analytes into GC-IMS. The LODs obtained for [Omim][PF_6]-extracted bromodichloromethane, bromoform, chloroform, and dibromochlorome-

thane were in the range 0.1–0.9 μg/L with reproducibility of 7.1% (RSD) [53].

4.4. Hollow-fiber liquid-phase microextraction

Another liquid-liquid extraction (LLE) method is HF-LPME [56–58], which has been developed from SDME by adding an HF, the function of which is to stabilize and to protect the drop of organic solvent, and thereby enhance the extraction efficiency. In practice, water-immiscible solvent (typically 5–30 μL) is placed inside the porous HF as a thin layer of supported liquid membrane (SLM) and the lumen of the HF is filled with a μL volume of acceptor solution. The acceptor is aqueous (three-phase mode) or the same organic solvent used in the pores of the HF (two-phase mode) [58]. Analytes are extracted from the aqueous sample through organic solvent to acceptor phase (Fig. 1). Thereafter, the acceptor solution is directly compatible with various analytical methods.

The HF-LPME method is suitable for extracting hydrophobic ionic analytes (i.e. basic or acidic compounds with ionizable functionalities). The two-phase method is also suitable for extracting neutral analytes. Both HF-LPME methods have been used in environmental applications to extract low polar analytes {e.g., pesticides, polyaromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) from aqueous matrices [57,58]}. The advantages of LPME are speed, low cost, and the possibility of high analyte enrichments because the analytes are extracted into a very small volume of the acceptor phase [57]. LPME can also be automated [56].

HF-LPME combined with IMS is also suitable for the determination of hydrophobic analytes from water, although it has been reported only in the analysis of biological matrices. Recently, LLLME-IMS was used in the determination of therapeutical drugs from urine and plasma samples [59–61]. In the latest HF-LPME-IMS study, CD-IMS was used to determine antidepressant clomipramine from human urine and plasma without additional sample pretreatments other than extraction. In the procedure, analytes were extracted to methanol acceptor from an alkaline sample solution through an HF membrane immobilized with *n*-dodecane. LLLME-CD-IMS was capable of determining clomipramine with the LOD of 0.35 μg/L and linear dynamic range of 1100 μg/L, and the results were comparable to other analytical methods. Also in this study, some carboxylic acids were investigated as novel reagent gases for improving the sensitivity of clomipramine analysis [59].

A similar procedure was used in another study, where two tricyclic antidepressant drugs, trimipramine, and desipramine, were determined from urine and plasma samples. In this study, analytes were extracted to an aqueous acceptor and determined with ESI-IMS. The method quantitation limits (MQLs) achieved were 5 μg/L for both analytes [60].

LLLME-ESI-IMS has also been used to determine an analgesic drug, pentazocine, in urine and plasma samples. In this procedure, the LOD of 2 ng/mL was achieved with an RSD of 5.3%. The linear calibration range was 10–500 ng/mL in this study [61]. As a consequence, LLLME-IMS provides prompt determination of drug analytes with comparable LODs.

4.5. Membrane extraction

The use of membranes is preferable because membranes can facilitate extraction without mixing two phases. Consequently, emulsion formation and high amounts of solvents are eliminated. Membrane separation can be divided into many application areas (e.g., reverse osmosis, microfiltration, ultrafiltration, PV, gas separation, and dialysis). In the extraction process, analyte molecules pass through the membrane with diffusion by concentration, pressure or electrical potential gradient. Membrane extraction can be performed by different configurations {e.g., supported liquid-membrane (SLM) extraction, microporous membrane LLE (MMLLE) or polymeric membrane extraction (PME) [12,28,62]}. This sub-section considers some applications of PV-type polymeric membranes suitable for IMS.

Membrane-based PV has most commonly been used in the dehydration of organic solvents, whereas it is more challenging to separate organic-organic solvent mixtures (e.g., polar/non-polar liquid mixtures, or isomers). PV has also been applied to the removal of trace volatile organic compounds (VOCs) from aqueous solutions [63,64]. In membrane-based PV extraction, the analytes are transferred across the membrane by concentration gradient from liquid to gaseous phase according to analyte permeability coefficients. PV can be seen as a three-step procedure, including partitioning of components from the donor to membrane, diffusion through membrane, and evaporation into the gas phase [28,63,64]. In comparison to other extraction methods, the advantages of membrane techniques are not only the selectivity, enrichment power, and automation potential but also the economic and occupational health aspects [62]. An inherent limitation of membranes is their sensitivity to solid contaminants [12].

Although membranes are widely demonstrated with IMS, membrane extraction has been combined recently with IMS in only a few studies in environmental analysis [65–69]. The latest studies focused on analysis of chlorinated hydrocarbons in water with membrane-extraction IMS (ME-IMS) [65,66]. A hollow PDMS membrane-inlet system was developed to extract tetrachloroethylene also known as perchloroethylene, (PCE) and trichloroethylene (TCE) from water, and IMS was capable of detecting 80 μg/L PCE and 74 μg/L TCE in negative-ion mode [65].

The feasibility of ME-IMS in the detection of trace levels of chlorinated hydrocarbons was also studied from the theoretical point of view. Mathematical modeling

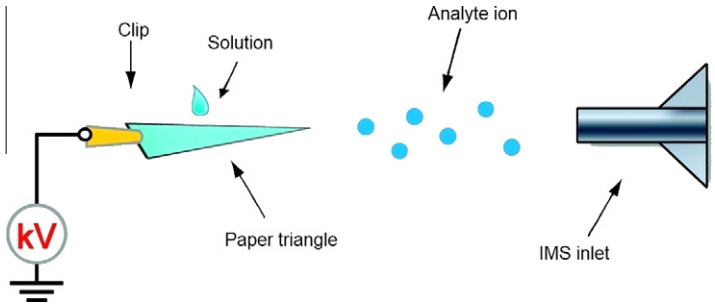

Figure 4. Paper spray in combination with ion-mobility spectrometry (IMS) analysis (Adapted and reprinted with permission from [70]. © 2010 American Chemical Society).

was used to consider TCE transport through the membrane by PV, and the model was able to fit the experimental observations [66].

The combination of a membrane sampling device and IMS has been reported for studies of water pollutants (e.g., benzene and MTBE) with different ionization techniques [67–69]. An active membrane combined with photo-ionization DMS (UV-DMS) was used to evaluate benzene from water in the presence of phenol, and this ''membrane in sample'' type of inlet with heating was capable of detecting 10 mg/m^3 of benzene [67].

In another study, flat silicon membrane produced in-house was used to extract MTBE prior to IMS detection, and sensitive detection of concentrations >10 μg/L was achieved with ^{63}Ni and UV ionization. The same experimental set-up achieved an LOD of 100 μg/L for the on-line procedure. The method was also capable of the quantitative determination of MTBE in the presence 30 wt% of BTEX compounds [68]. Furthermore, MCC IMS combined with membrane extraction was able to detect 20 mg/L MTBE with UV-ionization and 1 μg/L with ^{63}Ni-ionization in water [69].

4.6. Paper spray

Paper spray is a novel direct sampling method, which has been introduced for both MS and IMS [29,70,71]. IMS especially can be easily adapted to paper-spray ionization because both operate at ambient pressure. Paper spray is a variant of ESI, and it combines sample collection, analyte separation and ionization in open-laboratory environment. Paper spray can be described as a combination of paper chromatography and electrospray ionization. A small volume of sample solution (< 10 μL) is placed on the paper triangle and left to dry. The sample can also be transferred from the surface by wiping with paper. Analytes are separated by the distribution between paper and added solvent phase (capillary effect), and after the separation, ions are generated by applying a high voltage (3–5 kV) to the wetted paper through a copper clip [29,70]. At the moment, the transport and ionization mechanism of paper spray is not well described. Fig. 4 shows paper spray for IMS analysis.

The entire paper-spray analysis is fast, and results are available 1 min after sampling. Other advantages of this ambient pressure and temperature method are the potential of making disposable sample cartridges for analysis, low consumption of sample consumables required for the analysis, and untrained personnel can obtain immediate results for *in situ* analysis [29,70].

Paper spray, as ESI, is suitable for the determining of small organic compounds, peptides, and proteins from complex mixtures, and it is described for therapeutic drug monitoring from biological matrixes {e.g., blood and urine samples [29,70]}. Although paper spray combined with IMS is described for only biological samples, it also has potential for water matrices.

In a recent IMS study, paper spray was utilized in the determination of pharmaceuticals from urea samples [71]. The paper spray-IMS analysis of chlorpromazine resulted in an MH^+ product ion, the ion composition of which was confirmed with MS analysis. It was possible to detect the analyte with a drift-tube composition within the concentration range of 30–500 ng/μL with an estimated LOD of 1.5 ng/μL.

5. Conclusions

IMS offers a straightforward, low-cost option for fast, sensitive determination of organic pollutants. It is a suitable technique for the analysis of environmental samples (e.g., water) when coupled with sophisticated sample-extraction methods. However, applications published so far are still scarce in this field. The extraction methods and examples of applications described here have covered the full scale of recent research on IMS in water-quality analysis. There is a trend towards developing extraction methods that are easy to operate, capable of trace analysis with good sensitivity, and can be operated on-line. In combination with IMS, the extraction method should transfer the sample fast to the

gas phase and enhance the selectivity of IMS analysis in the case of complex matrices. Extraction methods interfaced to portable IMS analyzers are especially valuable when rapid, on-site analysis of water quality is required.

The methods described can perform real-time analysis, and most of them can be automated.

They have different numbers of sample-preparation steps and ease of use. Currently, SPME and membrane extraction are best suited for continuous determination of water pollutants by on-line analysis with automated sampling. The existing extraction methods for aqueous samples are suitable for various types of substances. For example, SPME and SBSE are feasible for non-polar and polar molecules. The development of new coating materials for SPME and SBSE could increase applicability to different kinds of samples.

Although HF-LPME and paper spray do not so far have a wide range of applications in water analysis, they possess the potential to determine proteins and therapeutical drugs from water matrices by IMS. For on-site analysis, low-cost sample-preparation methods (e.g., paper spray) could be ideal. As the most novel method, paper spray is also promising for paper-based microfluidic devices in combination with IMS. As a consequence, IMS is a potential method for on-site and on-line determination of organic pollutants in aqueous matrices.

Acknowledgement

This work was financially supported by Tekes – the Finnish Funding Agency for Technology and Innovation – and the Academy of Finland (Decision No. 124009).

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