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Review

On-line combination of aqueous-sample preparation and capillary gas chromatography

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Abstract

An overview is presented of methods currently in use to combine the preparation of aqueous samples on-line with capillary gas chromatography. Two approaches can be distinguished: heartcut-orientated reversed-phase liquid chromatography–gas chromatography (GC) and analyte-isolation-orientated analyte extraction–GC. These approaches either use techniques in which water is directly introduced onto the GC column, or an indirect approach in which water is eliminated, i.e., by solid-phase extraction, solid-phase microextraction or liquid–liquid extraction, prior to introduction of the analytes onto the GC column. The latter type of approach is much more successful and user friendly, and many applications have been reported. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Reviews; Sample preparation; Water analysis; Environmental analysis; Liquid chromatography–gas chromatography; Pesticides

Contents

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1. Introduction

In the past decade, analytical chemists have increasingly become aware that the combination of a single analytical column and a selective detector often does not suffice for the identification and quantification of the analytes of interest in their samples. Recently, therefore, *multidimensional* approaches came into focus to solve the many, and often complex, problems concerning the provisional identification of analytes of interest, the prevention of undesired coelution of other sample constituents and also because of the generally felt need to incorporate sample preparation on-line in the total analytical procedure. Two major branches have emerged, *hyphenation*, which may be defined as the on-line combination of a separation technique and a spectroscopic detection device which provides structural information, and *coupled-column* techniques, a term which does not require further explanation. Combining both approaches in one set-up self-evidently will further increase the potential of the analytical systems.

Recent years have seen exciting developments with regard to chromatographic instrumentation, automation and interfacing. Many of these contributed materially to the possibility to construct the multidimensional systems in use today. Still, even today, interfacing can create considerable problems. As regards hyphenation, this is true for, e.g., liquid chromatography–mass spectrometry (LC–MS), where – despite distinct progress – the ''universal interface'' has not been developed as yet, and for both LC–Fourier transform infrared detection (FT-IR) and gas chromatography (GC)–FT-IR, where deposition-based approaches do yield good analyte detectability but at the cost of the flexibility of operation. As regards coupled-column techniques, the on-line combination of liquid- and gas-based systems merits special attention. Again, over the past few years, great strides forward have been made.

To quote some examples, solid-phase extraction (SPE) [with either solvent desorption or thermal desorption TD)] can now be combined with GC almost on a routine basis which provides us with the powerful options of SPE–GC and solid-phase extraction–thermal desorption (SPETD)–GC. Next, the inherent problems of on-line RPLC–GC as contrasted with normal-phase LC–GC are much better understood, and have recently been reviewed in some detail [1,2]. Solid-phase microextraction (SPME)–GC has emerged as an alternative to SPE–GC, combining a greater ease of operation with a more restricted field of application. Finally, as we intend to discuss briefly in Section 5 of this paper, large-volume injection (LVI)–GC is an interesting alternative option: though the required coupled-column situation is absent here, the analytical result often is on a par with those of the systems considered above.

As was stated above, demands such as (i) improved analyte detectability and separation power – or sensitivity and selectivity – next to (ii) real-time confirmation of analyte identity and quantification, and (iii) the generally recognized need to increase sample throughput, have triggered the development of on-line, and preferably automated chromatography-based systems. The benefits of integrated analytical procedures – where the emphasis is on the inclusion of the sample preparation step – have frequently been discussed in the literature and need not be repeated here. However, when applying

multidimensional techniques to the trace-level determination of organic microcontaminants – which is what they are used for most often – there are two more aspects of interest to be considered, viz. the preferred separation technique, and the sample type of interest.

As regards the former aspect, it is generally recognized that GC should be one's first choice because of its speed of analysis and separation efficiency and because of the wide range of selective and sensitive detection methods available. From amongst these, the MS which provides excellent detection and identification possibilities for amounts of analytes of, typically, 0.1 ng or even less, merits special attention. However, even if one dismisses the problems of thermolabile or insufficiently volatile analytes, because these can often be remedied via derivatization, analysis by means of GC has one rather weak point: sample introduction. Until recently, and in many instances even today, the injection volumes often are a few microlitres only. Since, after suitable sample treatment, the volume of a final extract typically is between 50 μl and 1 ml, this implies that in the last step prior to GC analysis, some 95–99% of all analytes collected are simply discarded. For the successful performance of (ultra) trace analysis, it is of course highly advantageous to inject larger volumes. Fortunately, today the state of the art of injection techniques for GC is such, that with retention gaps gradually becoming standard equipment in many laboratories, the introduction of 10–100 μl volumes does not present a real problem any more, provided a suitable solvent such as, e.g., an alkane or ethyl acetate is selected. Techniques that have been developed to this end can, of course, also be used to transfer relevant fractions from a LC column or an SPE pre-column – and also from a dialysis or a continuous liquid–liquid extraction (LLE) module – on-line to a GC instrument. These techniques are partially concurrent solvent evaporation (PCSE) using an on-column [3] or the Autoloop [4] interface, fully concurrent solvent evaporation (FCSE) using a loop-type interface [5] and the use of a programmed-temperature vaporizer (PTV) [6]. For a detailed discussion of these interfacing techniques, the reader is referred to some recent reviews [1,7–9] and a book [10].

With the advent of proper liquid–gas transfer techniques, the potential of GC-based separation techniques in terms of analyte detectability (quantitative instead of minor-aliquot sample transfer) and sample throughput (on-line operation, automation) has markedly increased. However, the direct introduction of many polar organic solvents and, especially, water into a gas chromatograph still presents serious problems. Because of the global concern for the quality of our water environment and the consequent need for large-scale monitoring of surface, ground, drinking and waste water, and the distinct importance of other areas in which aqueous samples or sample extracts are often encountered such as, e.g., bioanalysis, techniques to solve the problem of handling aqueous samples in on-line SPE–GC, LC–GC, etc., are eagerly sought. If these can be made sufficiently user-friendly, one may expect a dramatic reduction, i.e., by one- or two-orders of magnitude, of the aqueous sample volumes required per analysis. In addition, there will be no need any more to use large volumes of organic solvents for LLE-type operations. In the present review various approaches will be discussed and it will be demonstrated that several viable solutions for the automated analysis of aqueous samples by means of GC exist.

2. On-line LC–GC-based techniques

Today, the on-line coupling of normal-phase (NP) LC and GC is a well developed and robust procedure which is used routinely in quite a number of laboratories, mainly for heartcutting operations (see, e.g., Refs. [9,11,12]). However, the development of on-line reversed-phase (RP) LC–GC with its partly aqueous effluents has been remarkably unsuccessful. The discussion to be presented below, will serve to outline the problems which still exist, but will also be used to indicate the close adjacency, and sometimes overlap, of heartcut-orientated RPLC and its much more successful counterpart, analyte-isolation-orientated SPE–GC.

The problems encountered when working with water-containing solvent streams mainly reside in the characteristics of the retention gaps that have to be used. At present, all retention gaps are silylated capillaries (or capillaries coated with Carbowax or OV-1701-OH) which are manufactured to produce a deactivated inner surface wall that can be wetted by organic solvents. Such retention gaps are commer-

cially available, and no problems are observed if organic solutions have to be introduced. Unfortunately, this is not true for water-containing RPLC eluents or aqueous samples. Wettability then is essentially absent irrespective of the type of retention gap selected. Furthermore, water causes problems during the LC–GC transfer of the analytes. The evaporation rate of water, and also that of methanol and acetonitrile, is low which makes the transfer of large volumes time-consuming. Thirdly, water and water-containing eluents are very poor solvents for creating useful solvent or phase-soaking effects.

Despite the inherently large problems, several groups of workers have come up with successful solutions. Fig. 1 shows that for the RPLC–GC approach, both direct and indirect (i.e., via extraction or sorption) introduction techniques have been used, while with analyte isolation-orientated approaches the indirect technique is used almost exclusively, as is to be expected. In the latter instance, three alternatives can be distinguished: classical LLE uses an organic solvent, with SPE an LC-type stationary phase is used as the sorbent, and rather novel approaches use a GC stationary phase to extract the analytes from aqueous samples. Finally, desorption-cum-LC–GC transfer can be carried out either by solvent or TD.

3. On-line RPLC–GC

3.1. Direct introduction of water

3.1.1. Micro-LC

In micro-LC, peak volumes are small and, consequently, so is the amount of water-containing eluent that has to be transferred. The low evaporation rate of such eluents, therefore, is also much less of a problem. Cortes et al. [13] transferred 7 μl of acetonitrile–water (65:35, v/v) to a 15-m raw fused-silica retention gap without severe distortion of the peaks of compounds eluting near the FCSE transfer temperature. As an application they determined the toxic bacteriostat, N-Serve, in corn extracts. With an injection volume of only 100 nl into the LC–GC system equipped with an electron-capture detection (ECD) system, the detection limit was 5–10 μg/l. Although the application was successful, the risk

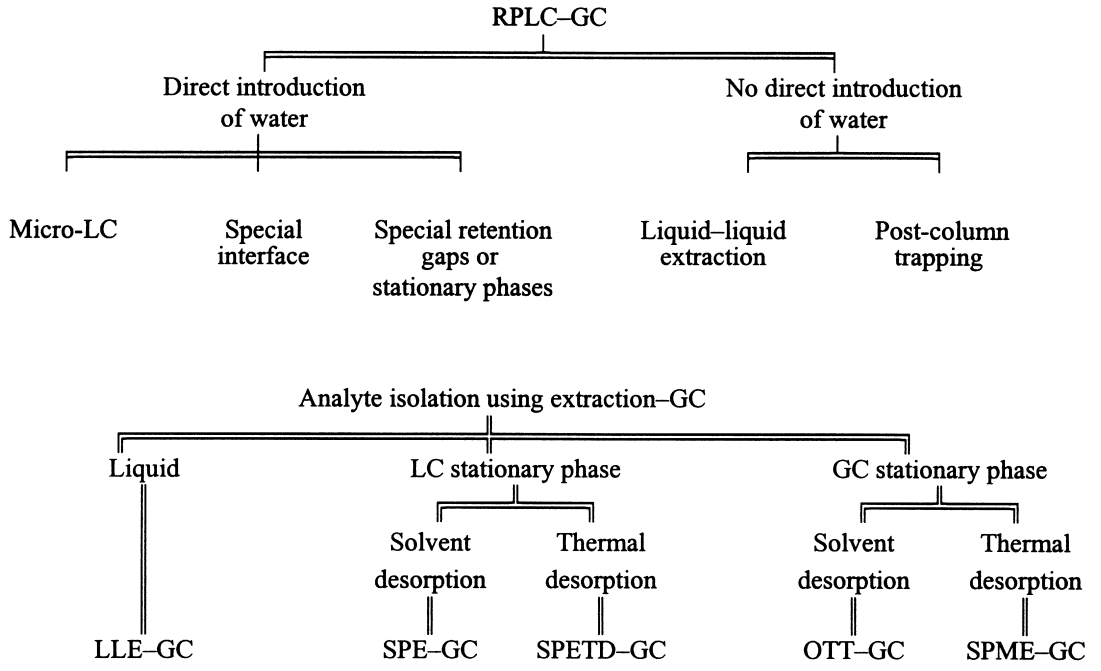

Fig. 1. Overview of approaches to interface LC and GC for aqueous eluents and samples.

remains that when using raw fused-silica, rather polar analytes will be adsorbed on the wall of the retention gap (see below).

3.1.2. Special interfaces

In principle the wettability problem can be overcome by transferring the aqueous eluent or sample above its boiling point via a loop-type interface. As an additional advantage, at the high temperatures used for the transfer, water will not destroy the surface of the retention gap. Grob, Jr. and Li [14] injected 10 ml of sample on an alkyl-bonded silica column, carried out the separation with methanol–water (60:40, v/v)+5% *n*-propanol and transferred the 150-μl heart-cut containing atrazine using FCSE into the GC system equipped with a nitrogen–phosphorus detection (NPD; detection limit, 3–5 ng/l) system. The transfer of aqueous eluents with a loop-type interface is, however, not too attractive because of the absence of solvent and phase-soaking effects. The method is therefore only suitable for compounds eluting at temperatures even higher than the usual 60–100°C above the transfer temperature or, in other words, the method is limited to the determination of compounds eluting at very high temperatures – in this case, atrazine.

More volatile compounds can be determined by adding a high-boiling organic co-solvent, such as butoxyethanol, which forms an azeotropic mixture with water. During transfer, part of the organic solvent remains in the retention gap and serves as a temporary stationary phase (solvent effect). Optimization of the co-solvent concentration and the transfer temperature have been described in some detail [15,16], but the technique has not been applied to real samples as yet.

Recently, Hyötyläinen and co-workers [17,18] reported the introduction of water-containing eluents from RPLC on-line into a GC system via a vaporizer chamber/pre-column solvent split/gas discharge interface. Water-containing eluents were transferred to a packed liner at 300°C. The vapour was removed by the carrier gas through a retaining pre-column and a solvent vapour exit (SVE). Loss of volatiles could not be prevented and the parameters determining such losses were studied in detail. The oven temperature during transfer was held close to the temperature at which recondensation occurs. The dew point depended on the transfer rate, the gas flow-rate, and the gas inlet pressure. Temperature measurements on the column outer wall enabled fast optimization of the most critical parameter, the transfer temperature. Recondensation of solvent inside the retaining pre-column increased the temperature on the outside. The method was applied to the determination of phthalates in drinking and surface waters (MS detection limits, 5–10 ng/l).

3.1.3. Special retention gaps or stationary phases

Duquet et al. [19] produced an aminopropyltriethoxysilane-deactivated retention gap which enabled them to introduce methanol–water mixtures, but data on peak asymmetry showed that the deactivation was destroyed; peaks of alcohols and methyl esters of carboxylic acids tailed badly. Pouwelse et al. [20] used a retention gap deactivated with a thin film of Carbowax (d_f=0.05 μm) and obtained good peak shapes when injecting 20 μl of acetonitrile–water (75:25, v/v) containing naphthalene and biphenyl as test compounds. They also used this retention gap for the transfer of water–acetonitrile mixtures under PCSE conditions with transfer flow-rates up to 100–230 μl/min [21]. The maximum introduction volume was 40 μl in a 5 m×0.53 mm I.D. retention gap. The LC eluents should at least contain 84% (v/v) acetonitrile (azeotropic composition) in order to prevent the remaining water to have an adverse effect. A dual-oven system was used because Carbowax can only withstand temperatures up to 250°C. Besides, when heating the first oven faster than the second one, a cold-trapping effect helps to obtain sharp peaks. More recently, a SVE was included in the system [22]. This increased the maximum injection volume to 200 μl, and the practicality of the system for RPLC–GC was demonstrated by on-line heart-cutting of the phenanthrene-containing fraction from a 2 mm I.D. LC column, and analysing it by GC and flame ionization detection (FID). The same authors also studied anion-exchange membranes to remove an ion-pair reagent from the LC eluent prior to transfer of a heart-cut to the GC [23]. The ion-pair reagent, methanesulphonate ions, was removed by exchanging it for (tetrabutylammonium) hydroxide ions (efficiency, 99.9%). This enabled direct introduction of the LC eluent, ''free'' of ions, into the GC system. The same

approach was used for the GC–MS identification of impurities in the drug substance mebeverine [24]. Fig. 2 shows the LC–GC–MS chromatogram and EI and CI spectra of mebeverine. Grob and Artho [25] could not reproduce the above type of results and concluded that there are no retention gaps capable of resisting water. Earlier they demonstrated that deactivated retention gaps lose their inertness after several injections of water-containing solvents [26–28]. Apart from the obvious controversy, the general experience is that the mixture of water and the organic solvent should evaporate azeotropically [27].

Van der Hoff et al. [29] reported promising results for a water-resistant retention gap which was coated with a 1-nm film of OV-1701, a water-resistant GC stationary phase. As an example Fig. 3 shows the chromatograms of the GC analysis of the Grob mixture using a 5 m×0.53 mm I.D. OV-1701-coated retention gap which was treated with water-containing ethyl acetate at 50, 80 and 100°C. A commercial version of this retention gap was used by Hankemeier et al. [30] who reported the absence of peak tailing with the Grob test mixture after the introduction of water-containing organic solvents.

Audunsson [31] reported the direct transfer of water onto a GC column packed with Pennwalt 223 with 4% KOH on Gas-Chrom. He developed a method for automated sample preparation using liquid membrane extraction for clean-up and trace enrichment of amines in urine samples. *n*-Undecane was immobilized on a PTFE membrane in which the neutral amines are trapped. Next, the amines were accumulated into the stagnant (or slowly flowing) acceptor buffer of low pH, their protonation preventing back-extraction into the donor channel (enrichment factors, up to 15). After mixing with 0.1 *M* NaOH, 3.5 μl of the resulting mixture were injected and analysed by GC–NPD (detection limits, low μg/l level; overall repeatability, better than 4%). Over 600 analyses were performed without deterioration of the membrane or the GC system.

3.2. No direct introduction of water

3.2.1. RPLC–LLE–GC

In an on-line set-up which includes a LLE step, the differences between a heart-cut operation (injection of a small volume of an aqueous LC eluent) and injection of an aqueous sample become rather small and, in the technical sense, even trivial. All procedures involving such a step are therefore discussed below.

3.2.2. RPLC–trapping column–GC

Next to the use of SPE as a pre-separation sample treatment step, which will be discussed in detail below, SPE has also been used to interface RPLC and GC by using an SPE cartridge as a post-column trapping column [32]. The LC fraction of interest was led through the cartridge and the analytes were trapped. After displacement of the water–methanol (20:80, v/v) used as eluent by water, the solutes were desorbed and transferred with ethyl acetate. With modestly retained compounds, and when analysing rather large LC fractions, the post-column addition of water helped to prevent analyte breakthrough. The system was studied with polynuclear aromatics as test compounds. Even when trapping a 2-ml fraction, recoveries of 98–100% were obtained after desorption and GC–FID analysis. Compared with RPLC–LLE–GC the approach has the distinct advantage that only small amounts of organic solvent (50–75 μl) have to be used. Both approaches share the advantage that LC eluents can be tolerated which contain buffers and water-soluble salts, since these are either not extracted or flushed to waste.

3.3. Conclusion

The above discussion clearly demonstrates that the heartcut RPLC–GC approach, even though the applications reported may be interesting and successful by themselves, has serious limitations, especially in terms of the volume of the fraction analysed and the LC eluent composition. Despite the many attempts, interfacing still creates problems and the technique still is in an exploratory stage. Actually, it is interesting to note that the alternative providing the widest choice of operating conditions utilizes an SPE cartridge, although in the post- rather than the pre-separation mode. For the analysis of large-volume aqueous samples containing many different types of analytes, one obviously has to look elsewhere for an adequate solution.

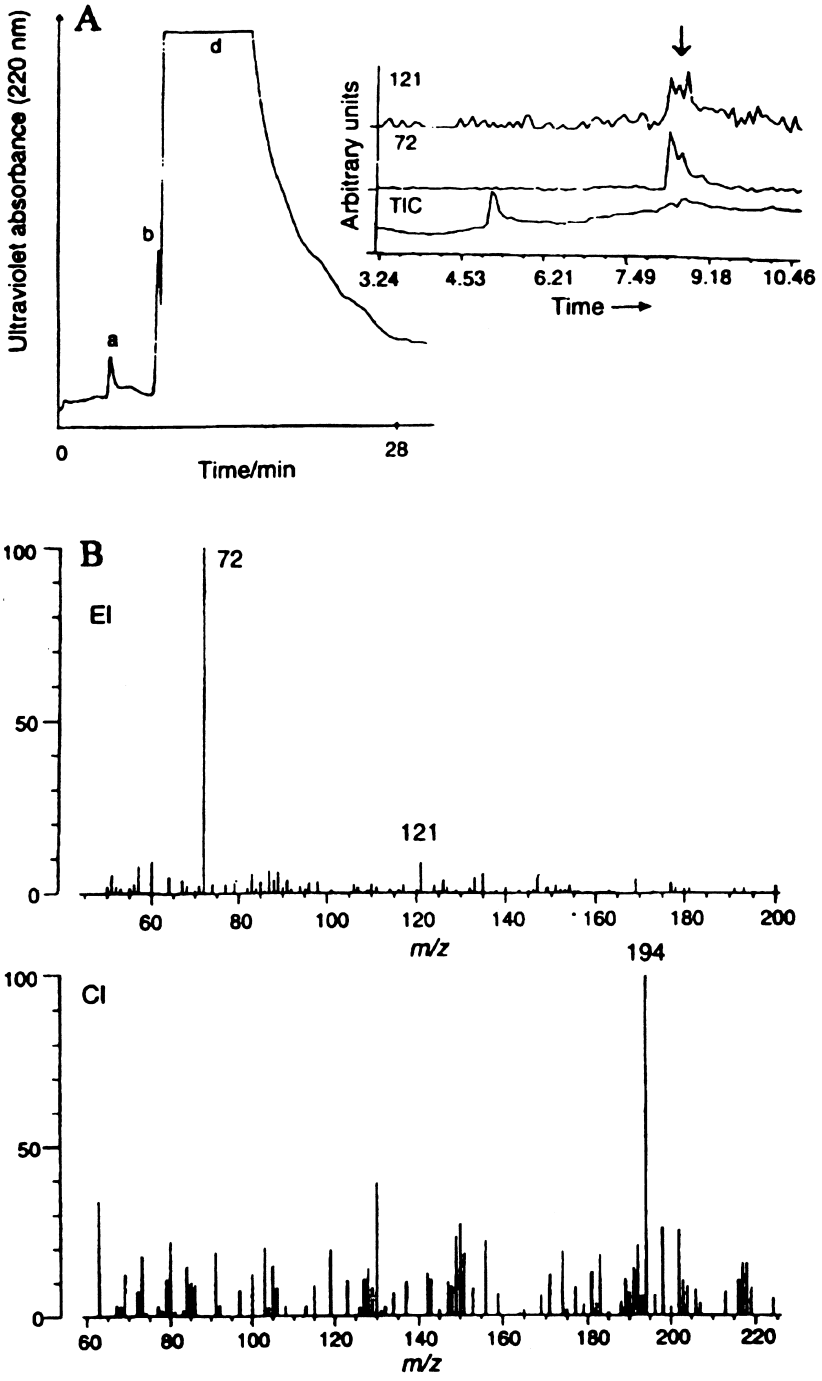

Fig. 2. (A) LC–UV chromatogram of a mixture containing 25 g/l mebeverine (d) and 25 mg/l (0.1%, w/w) of mebeverine amine (b) and veratric acid (a) after cation micromembrane suppressor passage with a TIC and extracted ion chromatograms (m/z 72 and m/z 121) of the transferred mebeverine amine fraction (about 5 ng) obtained by LC–GC–MS. (B) The pertinent EI and CI spectra of the transferred mebeverine amine fraction [24].

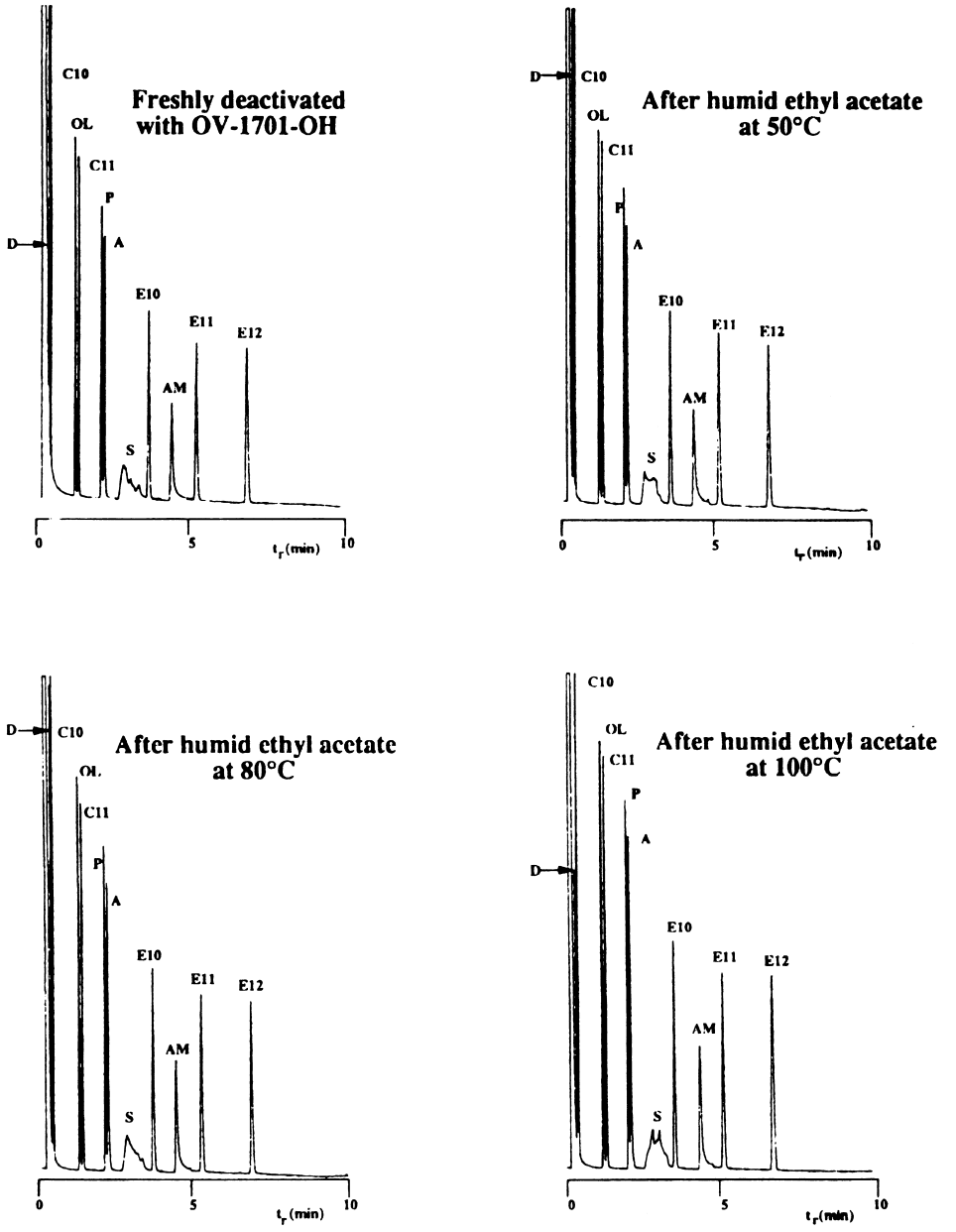

Fig. 3. GC analysis of the Grob test mixture using a 5 m×0.53 mm I.D. retention gap deactivated with OV-1701-OH. Peak designation: D=butanediol; C10=*n*-decane; OL=1-octanol; C11=*n*-undecane; P=2,6-dimethylphenol; A=2,6-dimethylaniline; S=2-ethylhexanoic acid; AM=dicyclohexylamine; E10–E12=methyl esters of corresponding carboxylic acids [29].

4. On-line analyte extraction–GC

4.1. LLE–GC

In an on-line LLE set-up [33–35] the aqueous sample is periodically injected into the organic solvent. The combined streams flow through a PTFE or fused-silica capillary, where a segmented flow is formed. Phase separation is achieved using a semi-permeable membrane or a sandwich-type phase

separator [36]. After plateau conditions have been reached for the extraction of the analytes, the organic phase is led through an interface and a suitable portion is transferred to the GC system. The basic equipment for on-line LLE–GC is shown in Fig. 4, in this case with a loop-type interface. It consists of two pumps, a segmenter which is usually a T-piece, an extraction coil, a phase separator and a valve which connects the extraction system to the gas chromatograph.

The total performance of a LLE–GC system depends on the characteristics of the extraction procedure: equilibrium should be achieved and analyte extraction should, preferably, be quantitative in order to increase detectability (and improve precision). Since the organic/aqueous phase ratios in the systems under discussion are generally close to unity, the fraction of an analyte that is extracted during the single-stage operation, θ, is given by

$$\theta = 1 - \frac{1}{1 + K_D} \quad (1)$$

where K_D is the distribution constant. K_D values should be larger than about 10 for all compounds of interest – a demand that is not easily met when such compounds cover a wide polarity range, as will often occur in actual practice.

Finally, one should be aware that, with real-life samples, the formation of emulsions may create problems and that high-purity organic solvents should be used as extractants. Adsorption of analytes to the inner wall of an extraction coil can generally be prevented by proper selection of the construction material.

4.1.1. LLE–GC applications

Roeraade [33] used LLE–GC for the automated monitoring of volatile organic trace compounds. The aqueous sample was continuously pumped through the system, and was extracted with *n*-pentane. Separation of the two phases was accomplished with a porous PTFE membrane separator. A 150-μl volume of the *n*-pentane fraction containing the analytes were transferred to the GC system. The on-line system showed better repeatability data than the batch extraction set-up. A similar set-up was used for the determination of halocarbons in seawater [34], organochlorine pesticides in ground water [35], and two pesticide intermediates, so-called NCC-ether and ACC-ether (for structure see Fig. 2 of Ref. [37]), in water in a toxicity study with water fleas.

Goosens et al. [38] also presented an on-line LLE–GC system which involves simultaneous extraction and derivatization. Organic acids could be alkylated in the two-phase system by analyte associa-

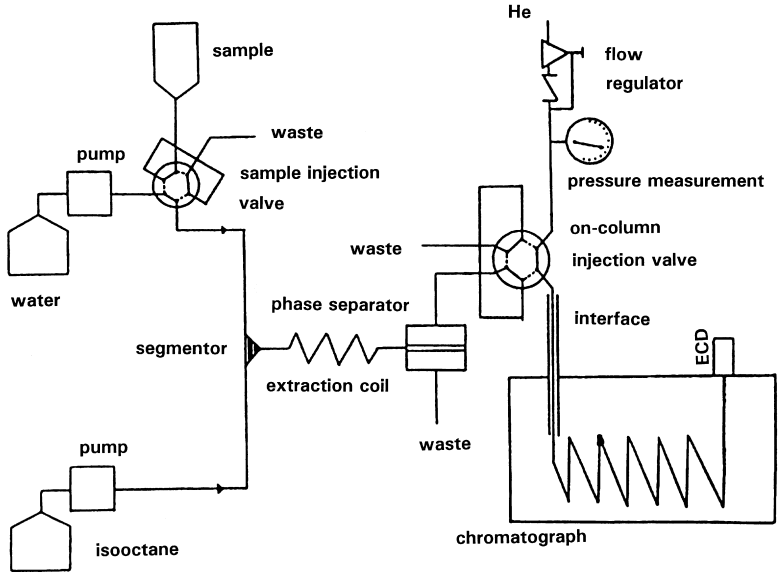

Fig. 4. Schematic diagram of set-up for on-line LLE–GC [35].

tion with a tetraalkylammonium ion, and ion-pair extraction into the organic phase, where alkylation takes place. Anilines could be acylated at the boundary between the organic and aqueous phases. With this set-up the authors were able to enhance the extraction yield and to improve the chromatographic behaviour of the polar solutes. A disadvantage was the presence of a rather large peak in the GC chromatograms due to the excess of reagent present in the organic solvent. More recently, a similar on-line LLE–GC system was combined with atomic emission detection (AED) for the detection of several nitrogen-, chlorine- and sulphur-containing pesticides in aqueous samples [39]. Relative standard deviations (RSDs) for the total LLE–GC–AED system were 2–4%. Ground water samples were screened and several contaminants could be provisionally identified on the basis of element response ratios.

Another continuous extraction system with and without two-phase derivatization was developed by Ballesteros et al.; it was used for the determination of phenols [40,41] and *N*-methylcarbamates [42] in water. The basic aqueous phase which contains the hydrolysis products of the aryl *N*-methylcarbamates was mixed with ethyl acetate for extraction and with *n*-hexane–acetic acid anhydride (100:8, v/v) for simultaneous extraction and derivatization. Four μl of the extract were stored in a loop and introduced into the GC injector by the carrier gas via a heated transfer line. The FID responses of the six pesticides were linear in the 0.1–160 μg/l range with RSDs of 2–4%. The system was also combined with ECD for the determination of the phenolic hydrolysis degradation products of *N*-methylcarbamates in milk [43]. The detection limits of the pentafluoropropionic anhydride derivatives were as low as 2–20 μg/l.

An alternative to using a phase separator is the at-line combination of automated micro-LLE and capillary GC [44]. A 1.5-ml aqueous sample was extracted with 1.5 ml methyl *tert*.-butyl ether in a sample vial of an automated sample preparation with extraction columns (ASPEC) system. Mixing of the sample and the extraction solvent was performed by repetitive drawing up and subsequent dispensing into the sample vial. Five hundred μl of the extraction solvent were transferred to the GC via an on-column interface equipped with a SVE. The system was used for the determination of organophosphorus pesticides (OPPs) in pond water with GC and flame photometric detection (FPD). In most cases, recoveries were over 70%; the detection limits were invariably at or below 0.1 μg/l. Although not yet fully automated with respect to sample preparation, LLE in an autosampler vial has also become very attractive. Extraction is carried out after addition of an appropriate organic solvent to the aqueous sample by gentle shaking. Miniaturization ensures that sample volumes can be very small and that the amount of organic solvent is, consequently, also small. A major part of the extract (up to 500 μl) can be injected into the GC system. By using special autosampler features, viz. adapting the insertion depth of the syringe needle in the vial, this part of the procedure can be automated. Optimization of the PCSE conditions has to be performed if volatile analytes are of interest [45]. Venema and Jelink [46,47] added 1 ml of *n*-pentane to a 2.5-ml autosampler vial containing 1 ml of aqueous sample, which then was closed with a crimpcap. After 3-min shaking, the vial was placed in the autosampler and 140 μl of the extract were injected. Hexachlorobutadiene and hexachlorobenzene were detected at 6 ng/l using MS detection in the selected ion recording mode. A similar approach was used for the determination of phenolic compounds in water [48] and anilines in industrial waste water extracts [49].

It will not come as a surprise that systems which are virtually identical to those used for LLE–GC, have been used for RPLC–LLE–GC (cf. above). In one application [50] the LC eluent was extracted with *n*-pentane and a 200–800 μl heart-cut containing fenpropimorph, that had to be determined in an aqueous cereal extract, was transferred to a GC–NPD system (detection limit, 10–20 ng/g). Ogorka et al. [51] used the same approach as an alternative to LC–MS, since LC–MS is less sensitive than GC–MS and (unless LC combined with tandem MS or MS^n techniques are used) does not produce spectra that can be used for identification. An unknown impurity observed during LC of a stressed sample of a pharmaceutical product was identified by directly transferring the LC fraction of interest to the GC–MS system. In a further study, an on-line derivatization step was included in the system. Degradation products obtained under severe alkaline stress of the drug substance ENA 713 were identified

as 3-hydroxyacetophenone and 3-hydroxystyrene. The degradation products were derivatized by trimethylsilylation and bromination. The usefulness of the technique was further demonstrated by the methylation of carboxylic acids with diazomethane and the extractive benzoylation of 2,6-dimethylaniline [52].

More recently, Hyötyläinen et al. used a similar set-up for the determination of codeine and β-blockers in urine [53]. Urine samples were directly injected onto the LC column; the only manual pretreatment was filtration of the sample. The LC fraction of interest was extracted with dichloromethane from which a 420-μl fraction was transferred to the GC–FID system via a loop-type interface. By means of co-injection of a derivatization reagent the analytes were silylated in the retention gap. The set-up was similar to that of Fig. 4, but the aqueous-phase pump was replaced by an LC system. Fig. 5 shows the LC–UV and the RPLC–LLE–derivatization–GC–FID chromatograms of codeine and β-blockers in urine (5–6 mg/l). The RSDs of the peak areas were 6–10%, and of the retention times, 0.05–0.4%. The sample preparation time (45 min) was considerably less than for conventional manual off-line procedures (2–3 h).

4.2. SPE–GC

On-line trace enrichment by means of SPE using so-called pre-columns or SPE cartridges is the most popular column-switching technique in LC. Pre-columns typically have dimensions of 1–4.6 mm I.D. and 2–10 mm length. In a large majority of all cases – whether these are LC- or GC-type applications – the pre-column is packed with 10–40 μm sorbents such as C_{18}- or C_8-bonded silica or a styrene–divinylbenzene copolymer. More recently, the use of one or more small membrane extraction disks stacked in a specially designed holder [54,55] has been recommended, especially for use in GC (see below). A typical on-line SPE–GC set-up is shown in Fig. 6 [56].

After conditioning of the stationary phase in the pre-column – which usually involves flushing with methanol and, next, with water – a sample volume

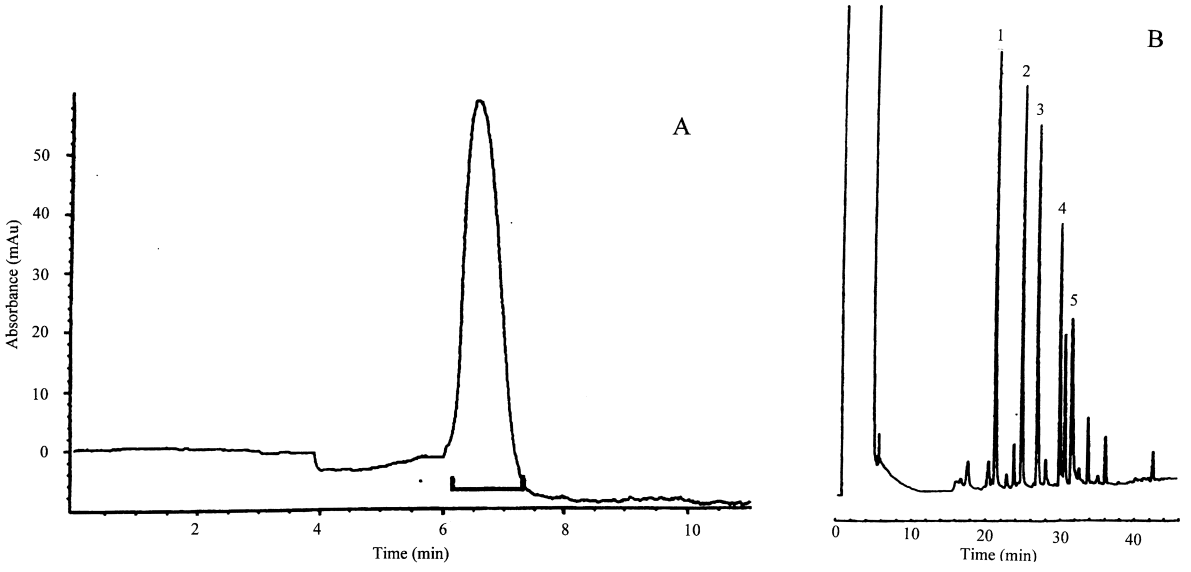

Fig. 5. (A) LC–UV chromatogram of spiked urine. Compounds: codeine (5.8 μg/l), metoprolol (6.0 μg/l), oxoprenolol (5.9 μg/l), propanolol (5.9 μg/l) and timolol (4.9 μg/l). Eluent, 0.05 *M* boric acid (pH 10.2)–acetonitrile (63:37, v/v); flow-rate, 0.8 ml/min. Extraction solvent: dichloromethane; flow-rate, 0.8 ml/min. UV detection at 240 nm. Transferred fraction, 420 μl. (B) RPLC–derivatization–LLE–GC–FID chromatogram of the LC fraction of interest. Peak designation: 1=oxoprenolol; 2=metoprolol; 3=propanolol; 4=timolol; 5=codeine. Temperature programme, 92°C for 8 min, at 15°C/min to 120°C (2 min hold), at 3.5°C/min to 220°C (1 min hold), 20°C/min to 280°C (5 min hold). Carrier gas, helium; flow-rate, 15.5 ml/min [53].

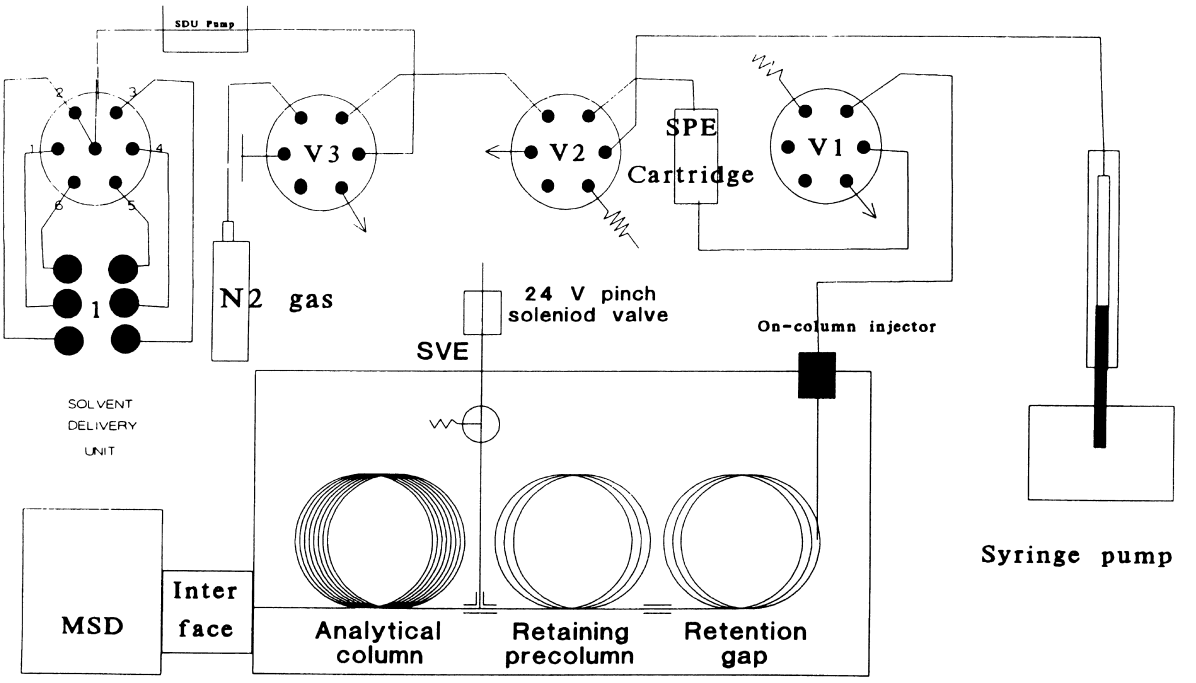

Fig. 6. Scheme of on-line SPE–GC system consisting of three switching valves (V1–V3), two pumps (SDU pump and syringe pump) and a GC system equipped with an SVE, an MS instrument, a retention gap, a retaining pre-column and an analytical GC column [56].

of, often, 10–100 ml in LC and, because of the better performance of GC detectors, of 1–10 ml in GC, is loaded at a flow-rate of 1–10 ml/min. The trace-level analytes of interest – and, also, many less desirable sample constituents – are preconcentrated on the pre-column; after clean-up by washing with, usually, HPLC-grade water the analytes are desorbed by the eluent used for LC separation (LC-type application) or by a suitable organic solvent (GC-type application) and, next, separated on the analytical column. The latter desorption procedure, which solely is of interest here, will be discussed below.

Loading sample volumes of several millilitres on a pre-column and subsequently transferring and analysing the total amount of analyte(s) retained on this pre-column, will cause a dramatic increase of analyte detectability expressed in units of concentration in the sample itself. However, selectivity is only slightly improved because of the non-selective hydrophobic interaction forces involved. If improved selectivity is a major goal (as it often is in LC), metal-loaded sorbents [57] or packing materials containing immobilized antibodies [58] can be used. So far these have hardly been used in GC with its superior separation efficiency and range of selective detectors.

It may be useful to add some more information about a main parameter of interest in trace-enrichment studies: the breakthrough volume, V_b, of an analyte on the pre-column used. It is evident that the sampling volume (plus the flushing volume; tests should be carried out with real-life samples) should always be smaller than V_b which can be calculated from the following equation [59]:

$$V_b = V_{o,p}(k+1) - 3\sigma_{v,p}$$
$$= V_{o,p}(k+1)\left[1 - \frac{3}{\sqrt{N_p}}\right] \quad (2)$$

where $V_{o,p}$ is the void volume of the pre-column, k the retention factor of the analyte on this column, $\sigma_{v,p}$ the standard deviation of the Gaussian peak eluting from the pre-column and N_p the plate number of this column. Although three parameters can, in principle, be adjusted to increase V_b and, thus,

enhance analyte detectability, viz. $V_{o,p}$, k and N_p, in actual practice neither the void volume nor the plate number can be sufficiently manipulated. In other words, the only option is to increase the retention factor. This readily explains why the well-known combination hydrophobic packing material/aqueous sample is such a good choice to preconcentrate organic compounds.

For the present discussion, it may suffice to add that abundant literature information indicates that breakthrough volumes for almost all non-polar to medium-polar compounds on a (5–10) mm×(2–3) mm I.D. pre-column packed with an alkyl-bonded silica, a copolymer or a related sorbent will at least be between 10 and 100 ml, with copolymers such as PLRP-S typically providing 20–30-fold more retention than C_{18}-bonded silicas.

Initially, most attention was devoted to the set-up of an on-line SPE–GC system and the procedure to be used. The set-up used in the first paper [60] was essentially maintained in most of the follow-up work. At first, the SPE cartridge (4 mm×1 mm I.D.) was built-in in a six-port valve and packed with C_{18}-bonded silica. Later, because of difficulties with exchanging the packing material, the SPE cartridge was built between two ports of a valve or between two valves. At least three switching valves had to be used, one to switch between aqueous (conditioning and sampling) and organic (desorption) solvents, another to supply drying gas and the third one to direct the liquid or gaseous stream to waste or into the GC system via a permanently mounted transfer capillary. In order to achieve the widest application range, PCSE conditions are commonly used during transfer of the analytes from the LC-type pre-column to the GC system using some 50–100 μl of organic solvent.

Noij et al. [61] introduced the use of a SVE vapour exit into the set-up which enabled evaporation and removal of the solvent via a T-splitter installed in front of the GC column. Transfer of very large fractions became possible, since no liquid remained in the GC inlet but the application range was rather narrow, since analytes were only prevented from escaping through the solvent exit by cold-trapping on the stationary phase of the inlet section of the GC column. The application range was improved by using the SVE concept introduced by Grob et al. [62], which consists of a valve situated after some meters of a so-called retaining pre-column.

The relatively small breakthough volumes of polar analytes can be improved by using a copolymer sorbent rather than silica-based materials (cf. above). For desorption, ethyl or methyl acetate should be used instead of hexane [63,64]. For a 10 mm×2 mm I.D. pre-column, 30–50 μl of desorption solvent are sufficient for quantitative analyte recovery. In practice, 75 μl are used to create a safety margin and prevent memory effects. The robustness of the approach was shown by determining polar compounds such as nitrobenzene and *m*-cresol at the 0.1–10 μg/l level (FID) using only 1 ml of sample. As another example, Fig. 7 shows the direct (i.e., no derivatization) SPE–GC–FID of chlorophenols in river water.

Since hydrophobic sorbents provide little selectivity, immunoaffinity sorbents were studied to remedy this deficiency [65]. Because desorption from an antibody-loaded pre-column, typically, has to be carried out with several millilitres of methanol–water (95:5, v/v), it is impossible to connect such a pre-column directly with the GC system. Therefore, the eluate was diluted with HPLC-grade water and the mixture led through a conventional C_{18}-bonded silica pre-column. As a result of reconcentration by dilution, with the gain in breakthrough volume due to increased retention caused by the decreased modifier percentage outweighing the volume increase, the analytes were quantitatively trapped on this second pre-column. Desorption from this trapping cartridge and transfer into the retention gap were done as described above. The method was applied to steroid hormones in 5–25 ml of human urine. The detection limit for 19-β-nortestosterone was about 0.1 μg/l. Recently, a similar approach using the combination of an antibody-loaded pre-column and a PLRP-S-packed pre-column was used for the determination of triazines in river and waste water and orange juice. The detection limits were about 10 ng/l when 10 ml of waste or river water were analysed using NPD [66].

To improve the robustness of especially the drying part of the total SPE–GC procedure two approaches have been reported, viz. (i) the use of membrane extraction disks rather than an LC-type pre-column,

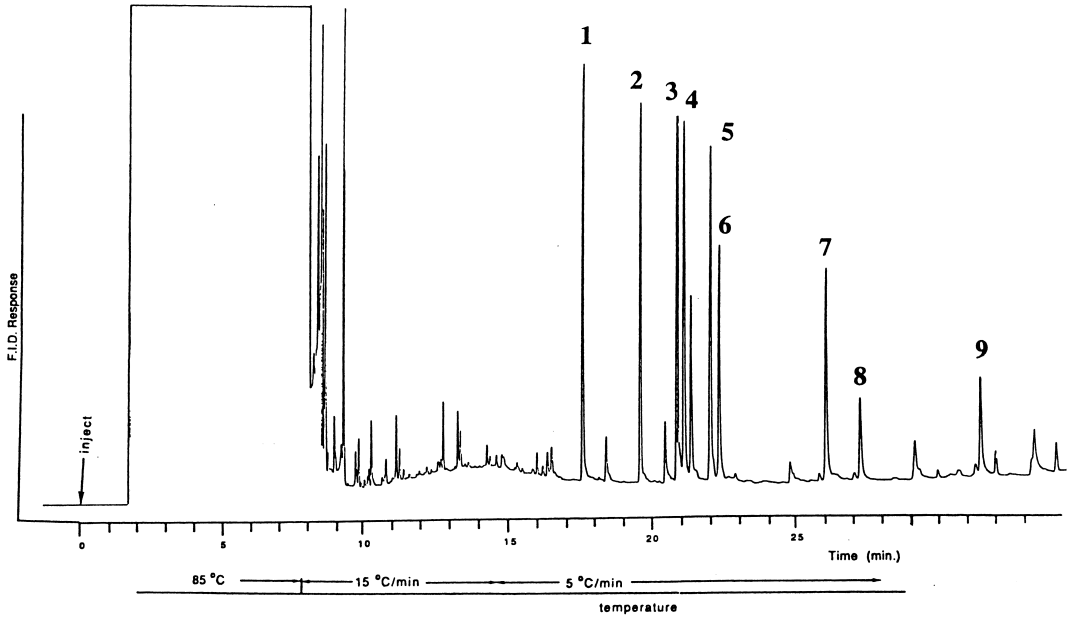

Fig. 7. SPE–GC–FID chromatogram of 1-ml River Amstel water spiked at the 10–40 μg/l level. Peak designation: 1=2,6-dichlorophenol; 2=4-chlorophenol; 3=2,4,6-trichlorophenol; 4=2,3,5-trichlorophenol; 5=2,3,6-trichlorophenol; 6=2,3,4-trichlorophenol; 7=2,3,5,6-tetrachlorophenol; 8=2,3,4,5-tetrachlorophenol; 9=pentachlorophenol.

and (ii) inserting a drying cartridge between the pre-column and the GC part of the system. With the former alternative three 0.5-mm thick, 4.6-mm diameter so-called Empore extraction disks which contain ca. 90% (w/w) of a polymeric packing material in a PTFE mesh (10%, w/w) [54] – were used instead of conventional pre-columns for the preconcentration of pesticides [55]. After sample loading, the disks could be dried by 10–15 min purging with nitrogen at ambient temperature. The system was shown to work well for the determination of OPPs in tap and river water (10–100 ng/l detection limits; NPD).

Drying based on purging of a pre-column or a stack of membrane disks is rather time consuming. An interesting alternative is to use a short drying cartridge containing e.g., sodium sulphate or silica, inserted between the SPE and GC parts of the system [67–69]. The drying agents should be reconditioned by heating after each GC run; they can then be re-used up to 100 times. Under suitable conditions, high recoveries and good RSD values have been obtained for, e.g., triazines, alkylbenzenes, chlorobenzenes and chlorophenols. In other words, analyte sorption on the drying agents is essentially absent even when working with sub-μg/l spiking levels. On-line SPE–drying–GC has been combined with FID, NPD and FPD and tap as well as surface waters have been analysed. In two recent studies, the design of the drying cartridge was improved to enable the use of higher temperatures during regeneration and to increase the efficiency of the packing material [70,71]. Several more volatile desorption solvents were studied to extend the application range at the ''volatile end''. From among the solvents tested, methyl acetate gave the best recoveries for both polar and apolar analytes eluted via a silica-packed drying cartridge, with tetrachloroethene being the most volatile analyte that could be determined successfully. Although drying agents, such as molecular sieves and sodium sulphate have a higher water retention capacity, silica was found to be the best choice under real-life conditions. With the improved approach, on-line SPE–drying–GC–MS was successfully tested with a mixture of 38 pollutants spiked to tap

water. Fig. 8 illustrates the potential of the approach and shows that low-ng/l detection limits can be achieved if selective detectors are used.

4.2.1. Analyte identification: SPE–GC–MS and other hyphenations

Next to low-level analyte detection by means of SPE–GC with various selective detectors, unambiguous identification at similarly low levels is, of course, a highly desirable option. Some early papers [72,73] demonstrated that on-line SPE–GC–MS can do just that. The system was used for the low-ng/l-level determination of atrazine and simazine in river water using either multiple ion detection or full-scan data acquisition with subsequent ion extraction. River water volumes of 1 ml and 10 ml, respectively, sufficed to detect and even quantify the analytes at concentrations of 30–100 ng/l (Table 1).

The above studies led to the development of an automated benchtop instrument, consisting of a Prospekt [Programmable On-line Solid-Phase E(K)xtraction Technique; Spark Holland, Emmen, Netherlands] for LC-type trace enrichment, drying of the membrane disk cartridge, and analyte transfer under PCSE conditions using a SVE, coupled on-line to a GC–MS system for separation and detection/identification [74,75]. The total system is software-controlled under Microsoft Windows and has been used to analyse water from many rivers and also greenhouse waste water [56]. To extend the application

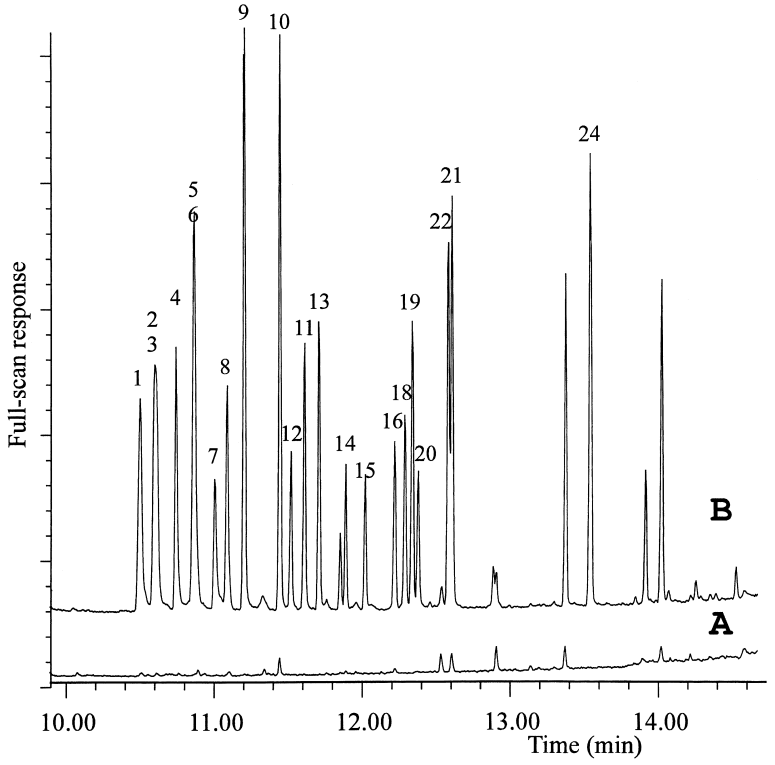

Fig. 8. SPE–drying cartridge–GC–MS (full-scan, *m/z* 35–435) chromatograms of 10 ml of Amsterdam tap water (A) without and (B) with spiking at the 0.5 μg/l level. Peak assignment: 1=3,4-dichlorobenzeneamine; 2=dimethylphthalate; 3=1,3-dinitrobenzene; 4=4-butoxyphenol; 5=acenaphthene; 6=3-nitroaniline; 7=1-naphthenelol; 8=pentachlorobenzene; 9=2,5-diethoxyaniline; 10=diethylphthalate; 11=1-nitronaphthalene; 12=1,2,4,6-bis-*O*-(1-methylethylidine)-a-L-sorbofuranose; 13=tributylphosphate; 14=trifluralin; 15=1,4-dibutoxybenzene; 16=hexachlorbenzene; 17=dimethoate; 18=simazine; 19=atrazine; 20=trichlorethylphosphate; 21=phenantrene; 22=diazinon (internal standard); 23=caffeine; 24=metolachlor [71].

Table 1
Concentrations of atrazine and simazine in water samples determined with SPE–GC–MS with full-scan acquisition (FS) and multiple ion detection (MID)[a]

Sample	Concentration atrazine (ng/l)				Concentration simazine (ng/l)			
	1 ml		10 ml		1 ml		10 ml	
	MID	FS	MID	FS	MID	FS	MID	FS
Drinking water (Amsterdam, June 1 1992)	25	25	15	10	15	nd	5	5
River Meuse (Eysden, February 4, 1992)	45	50	60	50	30	35	40	30
River Meuse (Eysden, June 19, 1992)	45	50	40	40	20	nd	15	15
River Meuse (Keizersveer, June 10, 1992)			370				240	
River Rhine (Lobith, April 22, 1992)	50	55	70	60	30	25	40	25
Limits of detection	5	30	0.5	3	5	30	0.5	3

[a] One- or 10-ml samples were used for trace enrichment; quantification was done at m/z 200 and 201 for atrazine and simazine, respectively. nd = Not detectable. If no value is given, the sample was not analysed in this mode.

range to apolar compounds such as organochlorine pesticides, 30% (v/v) of methanol should be added to the aqueous sample to prevent adsorption of the analytes to tubing and valves. It has to be added that – if analytes covering too wide a polarity range have to be determined in one run – usually a compromise has to be made between recovery of polar (pure water sample!) and apolar (high content of organic modifier!) analytes.

Pocurull et al. [76] demonstrated that the addition of modifier does not hamper the analysis of a group of medium polar herbicides and pesticides, although the most polar analyte in the test set (dimethoate) was almost completely lost after adding 30% of methanol to the sample. Fig. 9 demonstrates that the determination and identification of medium polar and apolar compounds is possible with selective ion monitoring (SIM) at the 0.1 μg/l level with only 10 ml of sample providing an excellent overall sensitivity and enhanced selectivity.

SPE–GC–MS has also been combined in one set-up with LC–MS. With a single sample handling unit and a single MS detector two sophisticated approaches were combined for the automated analysis of water samples [77]. With this multianalysis system, after trace enrichment of a 10–200 ml sample, the pre-column is eluted on-line in two subsequent runs, first to the GC–MS system and, next, to the LC–MS system using a particle beam (PB) interface. Both GC–MS and LC–PB-MS generate classical EI spectra which can be used for the identification of low- and sub-μg/l concentrations of micropollutants covering a wide polarity and volatility range. The limitations of GC–MS in terms of volatility and polarity were easily compensated by the LC–MS side of the instrument, while a large overlap in analyte detectability resulted in additional confirmatory data. With 100-ml samples, detection limits for a selected group of organochlorine pesticides in GC–MS were 0.5–30 ng/l, and in LC–PB-MS, 0.5–7 μg/l. The multianalysis system was also used to monitor the pollution at six sampling sites of the River Nitra over a period of two years [78]. In a follow-up study [79] it was shown that negative chemical ionization (NCI) MS, with methane as a reagent gas, caused the detection limits for six of nine target pesticides to improve 10–30-fold.

In the recent past, GC–ion trap detection (ITD) systems which can perform tandem MS (MS/MS) on a routine basis have become commercially available [80]. Because ITD provides very good sensitivity as well as increased selectivity in the MS–MS

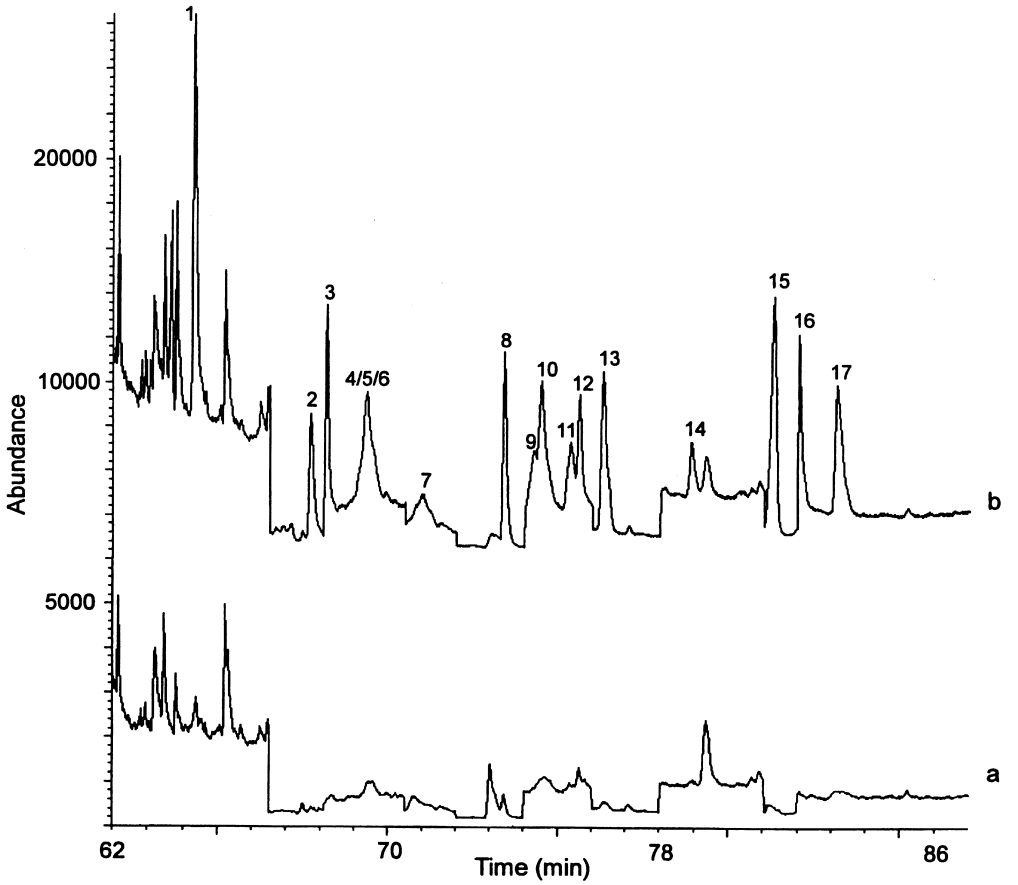

Fig. 9. SPE–GC–MS chromatograms of 10 ml of tap water obtained in the time-scheduled SIM mode (a) without and (b) with spiking at the 0.1 μg/l level. Peak assignment: 1=molinate; 2=α-HCH; 3=dimethoate; 4=simazine; 5=atrazine; 6=γ-HCH; 7=d-HCH; 8=heptachlor; 9=ametryn; 10=prometryn; 11=fenitrothion; 12=aldrin; 13=malathion; 14=heptachlor-endo; 15=α-endosulfan; 16=tetrachlorvinphos; 17=dieldrin. Retention times correspond to total analysis time including SPE and drying [76].

mode, an on-line SPE–GC–ITD system was optimized for the trace-level determination of polar and apolar pesticides [81]. The SPE–GC interface, an Autoloop, which operated at an injection temperature of 90°C also permitted the determination of thermolabile pesticides such as carbofuran and carbaryl. Linear calibration curves were obtained over the range of 0.1–500 ng/l, using sample volumes of 10–30 ml for enrichment on a copolymer SPE cartridge. The detection limits for the pesticides were 0.01–4 ng/l. Acceptable tandem mass spectra were obtained at levels as low as 0.1 ng/l level in real-life water samples. The system was used to analyse samples from the Rivers Rhine and Meuse, and Narmada (India). Fig. 10 shows the reconstructed SPE–GC–MS–MS ion chromatograms of desethylatrazine (75 ng/l), atrazine (130 ng/l), alachlor (8 ng/l) and metolachlor (16 ng/l) in Rhine water. Jahr [82] used SPE–Autoloop–GC–MS for the trace analysis of phenols in water at the low ng/l level. The phenols were derivatized by in-sample acetylation with acetic acid anhydride prior to fully automated SPE–GC–MS. The method was validated with 26 alkyl-, chloro- and mononitrophenols including 4-nonylphenol and 17-ethinyl-estradiol. Results showed good reproducibility and excellent sensitivity in the time-scheduled selected ion monitoring mode. Enoch et al. [83] used the Autoloop system in combination with GC–ECD for the extraction and determination of lindane, musk ketone and musk

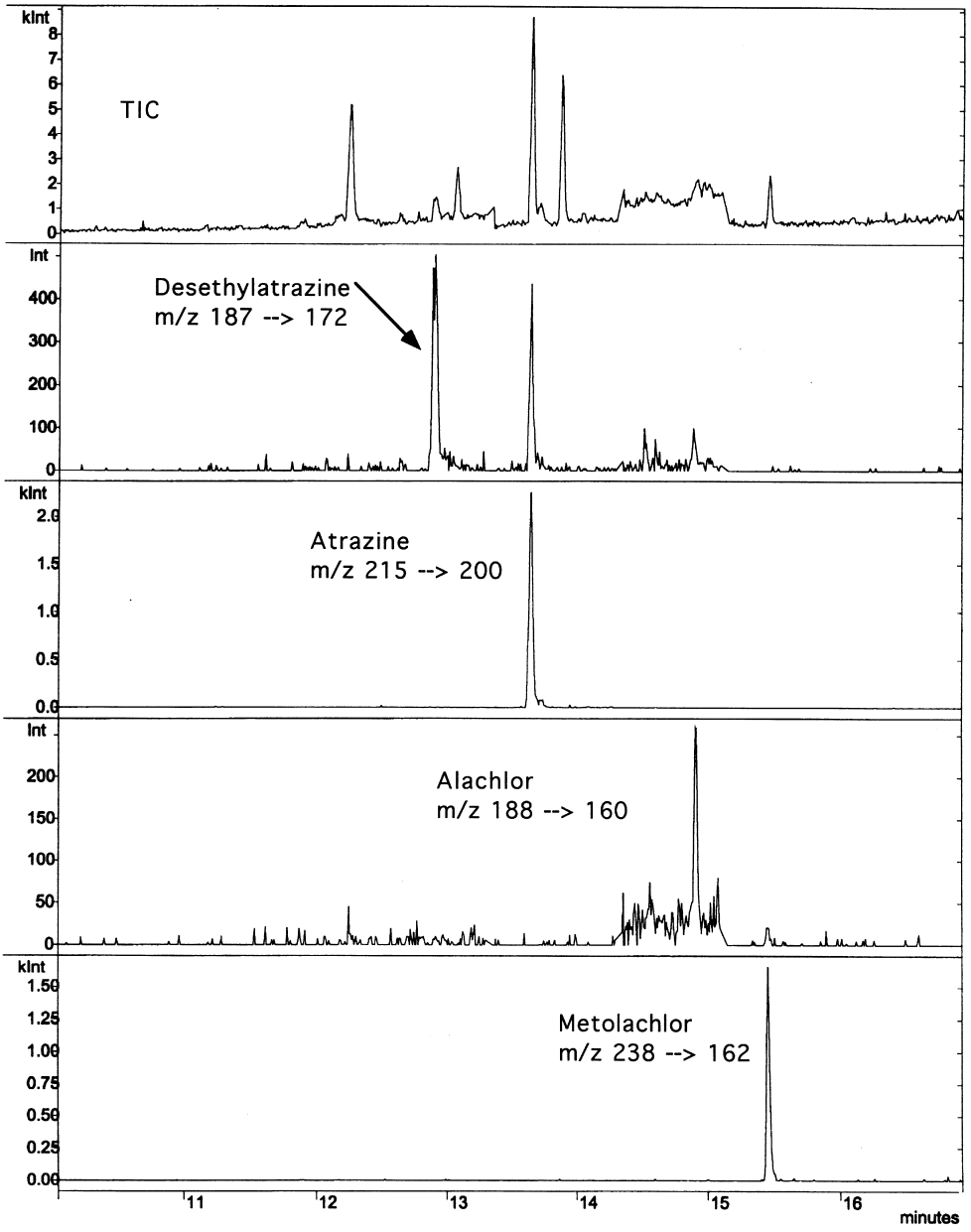

Fig. 10. Reconstructed ion chromatograms obtained after SPE–GC–MS–MS of 10 ml River Rhine water at *m/z* 172 (desethylatrazine), 200 (atrazine), 160 (alachlor) and 162 (metolachlor). TIC, total ion current [81].

xylene and reported detection limits at the low ng/l level.

In some early studies, SPE was combined off-line, i.e., via LVI, with GC–AED for the detection of OPPs in surface water, and for the confirmation of benzothiazole in the River Meuse [75] and triphenyl phosphine oxide in tap water [84]. Detection limits for the phosphorus channel were as low as 0.1 μg/l. Fig. 11 shows the carbon, nitrogen and sulphur traces of the confirmational GC–AED analysis of ben-

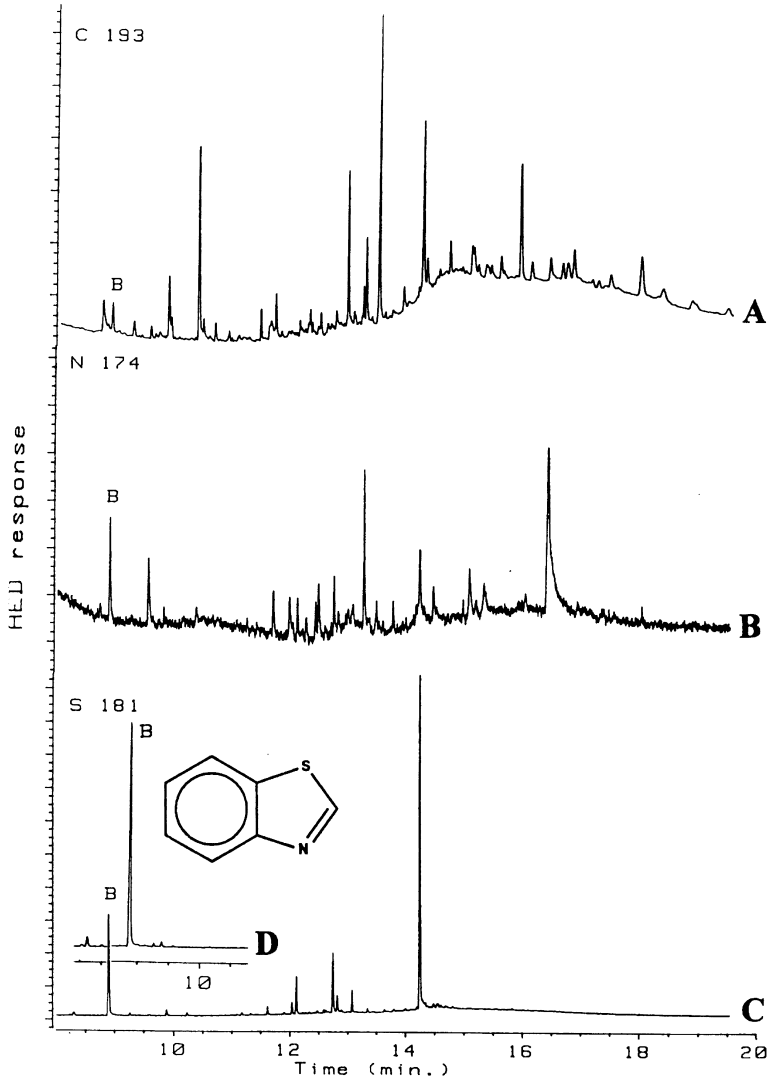

Fig. 11. GC–AED chromatograms of a 100-μl aliquot (20%) of ethyl acetate extract obtained after off-line SPE of 10 ml of River Meuse water; (A) C trace, (B) S trace, (C) N trace; (D) is the S trace of the chromatogram obtained after injection of 2 ng of benzothiazole in 100 μl of ethyl acetate [84].

zothiazole in the River Meuse water. Hankemeier et al. combined SPE on-line with GC–AED [85]. With 10-ml water samples detection limits of 5–20 ng/l were now obtained for the phosphorus channel. More recently, studies were published [86,87] in which SPE–GC is combined with simultaneous AED and MS detection. A procedure is proposed for the (non-target) screening of hetero-atom-containing compounds in tap and waste water, and in vegetable extracts. Target compounds as well as unknowns were identified, and quantified, above the predetermined threshold values of 0.05 (tap water) and 0.5 (waste water) μg/l.

Recently, there have been two successful attempts to combine LVI and SPE with GC–cryotrapping–IR [88,89]. The cryotrapping interface, with its GC effluent immobilization on a ZnSe window at 80 K and on-the-fly detection or post-run scanning, is rather sensitive to the presence of traces of water, but is some two orders of magnitude more sensitive than

the conventional light–pipe interface. To quote one interesting result on the on-line SPE–GC–IR set-up, sample volumes of only 20 ml sufficed to detect, and identify, microcontaminants in tap and surface water at the 0.1–1.0 μg/l level. When appropriate functional-group chromatograms were used, detection limits were as low as 15 ng/l for tap water. An interesting example is shown in Fig. 12.

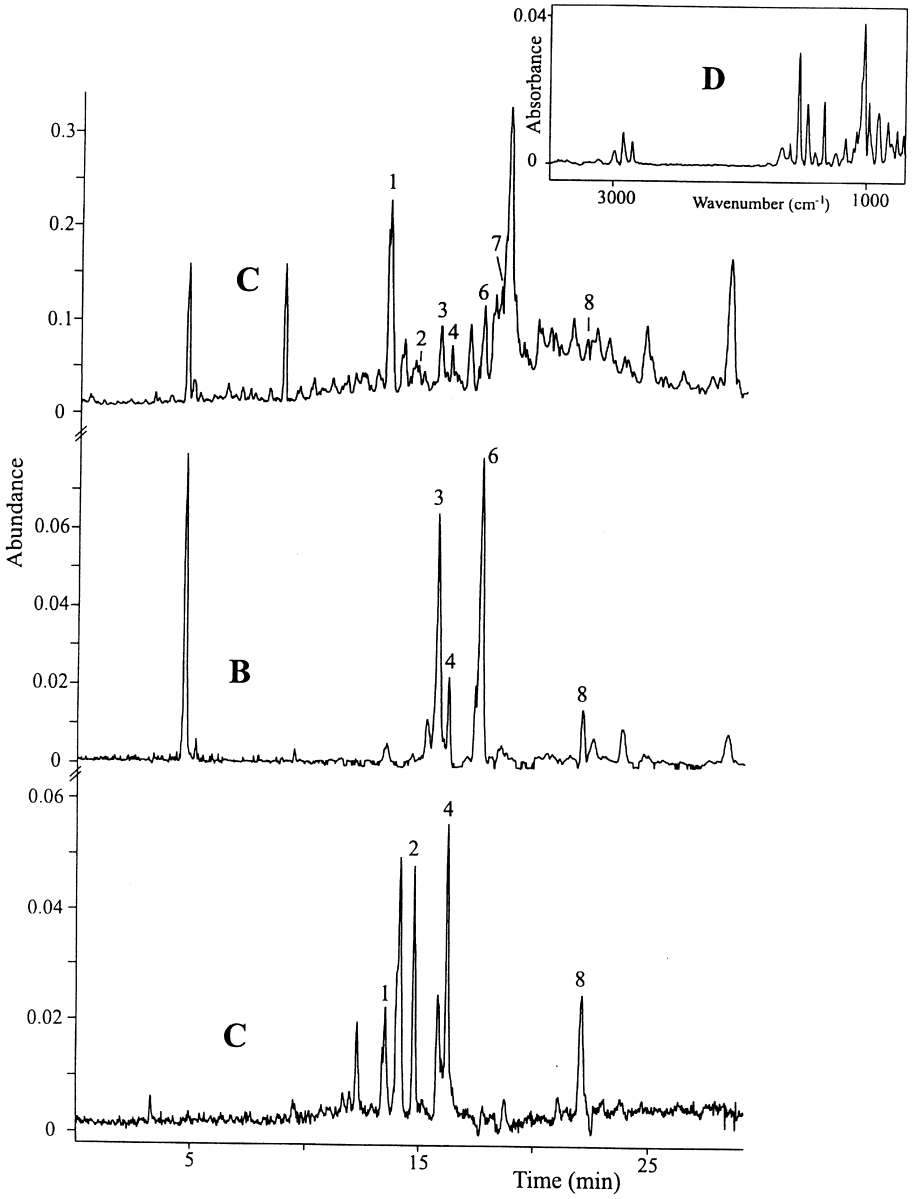

Fig. 12. On-line SPE–GC–FT-IR analysis of 20 ml harbour water spiked at the 1.0 μg/l level with several microcontaminants. The (A) Gram–Schmidt, two functional-group chromatograms, (B) (1520–1580 cm^{-1}) and (C) (1000–1050 cm^{-1}), and the (D) ''post-run'' IR spectrum of peak No. 8 are shown. Peak assignment: 1=diethylphthalate; 2=sulfotep; 3=atrazine; 4=diazinon; 5=caffeine; 6=simetryn; 7=metolachlor; 8=triazophos [89].

4.2.2. Analysis of volatile compounds

Considerable improvements with regard to extending the range of analysis at the ''volatile end'' were made by using a more volatile solvent, methyl acetate, and a presolvent in the SPE–GC approach using PCSE [90]. The problem of losing volatiles has been studied in depth [91,92]] and it was concluded that losses occur due to both the installation of a SVE and the use of PCSE conditions. In the new set-up [90], after conventional sample loading and drying with nitrogen, 30–50 μl of a presolvent (methyl or ethyl acetate) are introduced into the retention gap prior to the actual desorption to ensure the early formation of a solvent film. Analytes as volatile as monochlorobenzen and xylene are now easily recovered. The modified SPE–GC procedure was tested by analysing 10 ml of River Rhine water spiked at the 0.5 μg/l level with about 80 microcontaminants covering a wide range of volatility. Using test compounds such as chlorobenzenes, anilines, phenols and organonitrogen and OPPs, system performance in terms of recovery (typically 70–115% at the 0.5 μg/l level), repeatability (RSDs typically 1–9%; $n=7$) and detection limits (full-scan MS acquisition, 20–50 ng/l) were fully satisfactory, even for monochlorobenzene. Fig. 13 shows a chromatogram of spiked River Rhine water with this mixture.

4.2.3. ASPEC-based SPE–GC procedures

A rather different use of SPE–GC was described by Van der Hoff et al. [93] who used an ASPEC for the clean-up of concentrated organic surface water extracts – obtained by off-line LLE – to determine ng/l levels of pesticides. Fifty-ml surface water samples were manually extracted with 2 ml of *n*-hexane, and 50% of the extract was loaded on a 100-mg silica SPE cartridge (for clean-up). The

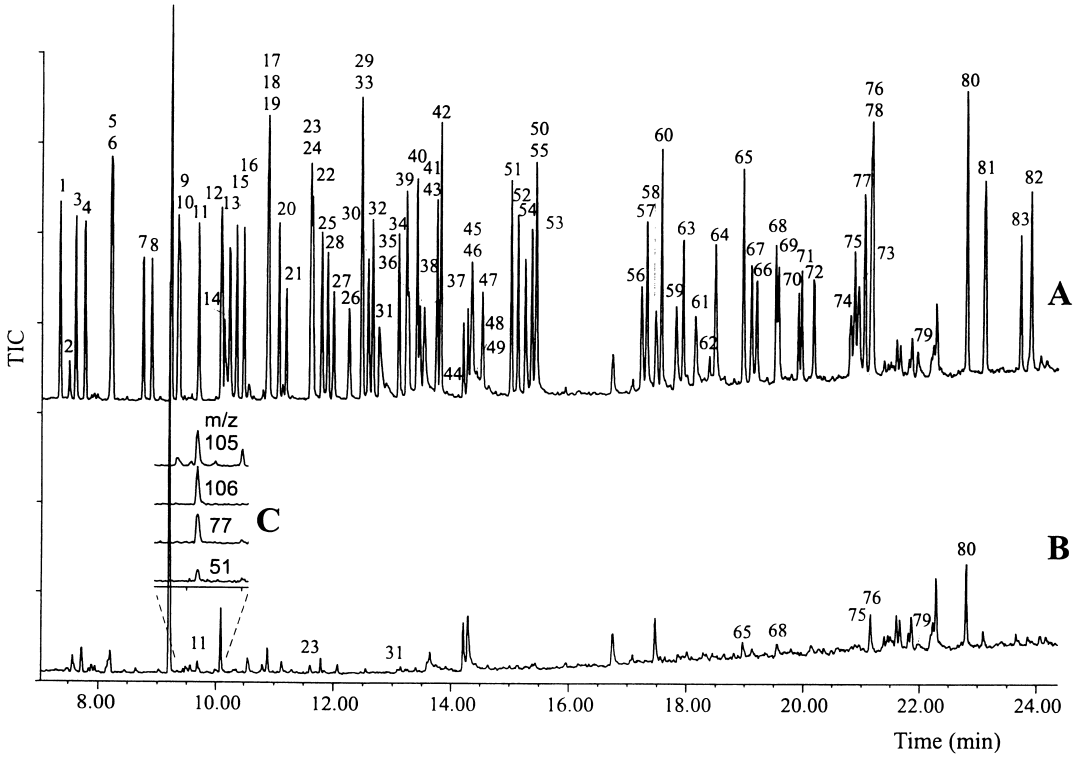

Fig. 13. Total ion current (TIC) chromatogram for SPE–GC–MS of 10 ml of River Rhine water (B) non-spiked and (A) spiked at the 0.5 μg/l level with 86 microcontaminants. Fifty μl of ethyl acetate was used as presolvent. The insert (C) shows four mass chromatograms characteristic of benzaldehyde (*m*/*z* 51, 77, 105 and 106); time scale for mass chromatograms twice as large as for TIC chromatogram [90].

analytes were eluted with 4 ml of *n*-hexane–2-propanol (99.9:0.1, v/v) and 200 μl from the final volume of 5 ml, were injected into the GC system via a loop-type interface. The analytes were recovered quantitatively and the precision was satisfactory. In a subsequent study the ASPEC system was used for automated SPE extraction and clean-up of pyrethroids in surface water [94]. The analytes were eluted with 1.5 ml of toluene from which 100 μl were injected into a GC–ECD system via an on-column interface. The detection limits were 1–8 ng/l; 30% of methanol had to be added to the sample to prevent adsorption to tubes and valves (cf. above). Fig. 14 shows a typical result for spiked (9–81 ng/l) tap water.

The trapping column–GC approach developed for on-line RPLC–GC (cf. above; [32]) was also used to interface an ASPEC system with GC. The clean-up of untreated plasma was carried out with disposable C_{18} cartridges, using several washing steps. After desorption with methanol, the extract was on-line diluted with an aqueous buffer and preconcentrated on a PLRP-S trapping column. After drying with nitrogen, desorption was carried out with 120 μl of ethyl acetate. With ASPEC–trapping column–GC–FID, the detection limit for the anti-depressant trazodone in plasma was 3 μg/l (1 ml sample). In a study on ASPEC–GC–NPD for the determination of benzodiazepines in plasma [95], the analytes were desorbed from the C_{18} columns with 2 ml of ethyl acetate. Instead of using a trapping column as an interface, a 100-μl aliquot of the ethyl acetate extract was injected via a loop-type interface. The limits of detection in plasma were 0.5–2 μg/l, and linearity and repeatability were fully satisfactory. As an extension, an automated derivatization step was included [96], with the determination of phenol and chlorinated phenols in water as an example. The analytes were acetylated with acetic acid anhydride, and the phenol acetates enriched on a copolymer SPE cartridge. After drying with nitrogen, the phenol acetates were desorbed with ethyl acetate and injected on-line into the GC–FID system under PCSE conditions. This enabled the determination of analytes as volatile as phenol acetate (RSDs for the integrated on-line procedure, 1–12% at the 1 μg/l level).

Szpunar-Lobińska et al. reported an off-line, but still very interesting, method using SPE, derivatization and LVI [97]. Ionic organotin compounds were preconcentrated on extraction disks at low pH. After derivatization at room temperature on the disks with

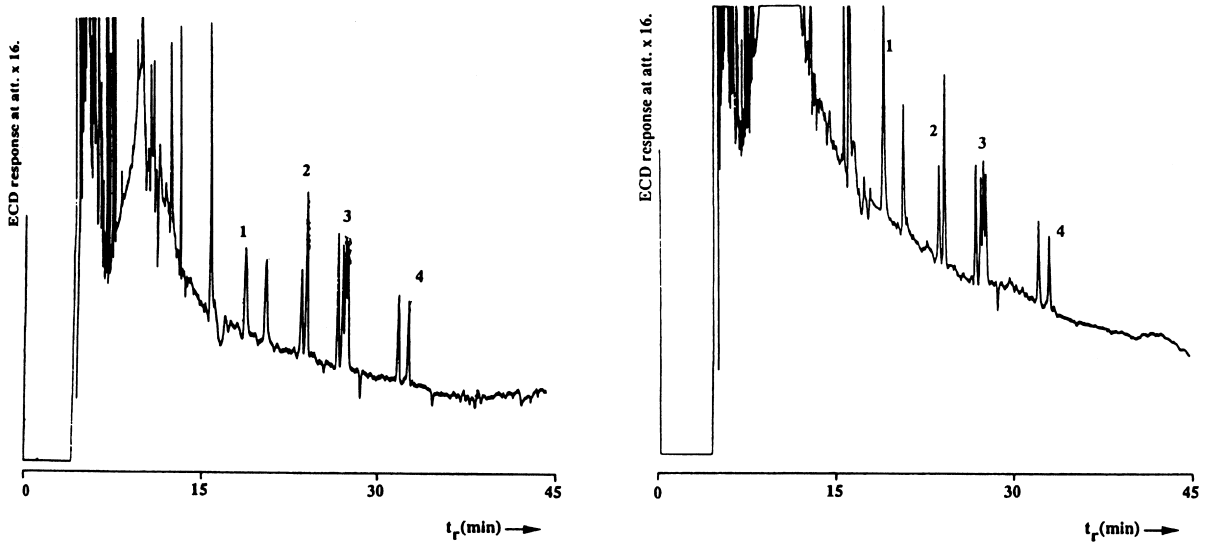

Fig. 14. Automated SPE–GC–ECD of a 19-ml tap water sample spiked with pyrethroids. Peak assignment: 1=fenpropathrin (17 ng/l); 2=mixture of *cis*- and *trans*-permethrin (54 and 81 ng/l); 3=mixture of *trans*-D-/*cis*-A-/*cis*-B-/*trans*-C-cypermethrin (13, 11, 9 and 16 ng/l, respectively) and 4=deltametrin (18 ng/l) [93].

tetraethylborate dissolved in an aqueous buffer (pH 9–10) and drying, the derivatives were desorbed with methanol and subjected to GC–AED. Analyte recoveries were quantitative except for the mono-substituted tin ions. Detection limits were 0.1–0.2 pg, which means that analyte levels of 0.1 ng/l can be detected with 50-ml samples. The injection was carried out after collection of the desorption solvent, but it should not be too difficult to set up a fully on-line system.

As an alternative to ASPEC–GC, on-line dialysis–SPE–GC was developed for the determination of drugs in plasma, again with benzodiazepines as model compounds [98]. Clean-up was based on dialysis of 100-μl samples for 7 min using water as the acceptor, and trapping the diffused analytes on a PLRP-S column. After drying, the analytes were desorbed with 375 μl of ethyl acetate which were injected on-line into the GC system via a loop-type interface. The system provides a very efficient clean-up, and offers the possibility of adding chemical agents which can help to reduce drug–protein binding. To demonstrate the potential of the approach, benzodiazepines were determined in plasma at their therapeutic levels. FID, NPD and MS detection were used.

4.2.4. Alternative phase-switching-based SPE–GC procedures

Noij and van der Kooi [99] developed a SPE–GC system with a loop-type interface and extended the application range at the ''volatile end'' by co-solvent trapping. The analytes were desorbed with 500 μl of methyl *tert*.-butyl ether–ethyl acetate (90:10, v/v). The eluate was injected together with 50 μl of *n*-decane which acted as co-solvent, and ensured the trapping of the volatile analytes in a solvent layer in the retention gap. With this approach OPPs as volatile as mevinphos could be determined.

Ballosteros et al. developed an SPE system for GC using the same interface as for on-line LLE–GC [100]. The analytes were extracted on XAD-2 styrene–divinylbenzene copolymer, dried for 3 min with nitrogen and desorbed on-line with 100 μl of ethyl acetate. Five μl of the eluate was stored in a loop and injected in a splitless injector via a heated interface capillary. When 50-ml samples were analysed by GC–FID, the detection limits of *N*-methylcarbamates and their phenolic degradation products were 0.7–1 μg/l. Subsequently, SPE–GC–ECD was used to determine chlorophenols [101]. With a 25-ml sample, the detection limits ranged from 2 ng/l (pentachlorophenol) to 10 μg/l (monochlorophenols). The system was used to detect many tri- and higher chlorinated chlorophenols in waste water.

Several successful attempts have been made to combine extraction, desorption and GC analysis using the Prepstation [102–104]. Hankemeier et al. [102] developed a fully automated at-line SPE–GC procedure for the analysis of aqueous samples. The sample extract is transferred from the sample preparation module to the GC via an autosampler vial. Final limits of determination (S/N 10) of 0.05–0.13 μg/l were obtained (FID) for a series of microcontaminants by systematically modifying the PrepStation procedure, viz. by (i) increasing the sample volume from 1.5 to 50 ml, (ii) changing to on-column LVI of 50 μl rather than 1 μl in the splitless or on-column mode, and (iii) decreasing the desorption volume to 300 μl by reduction of the amount of sorbent in the SPE cartridge. The potential of the system was demonstrated by determining triazines in River Rhine water at the 0.6 μg/l level using FID and MS detection. No practical problems were observed during the analysis of more than 100 river water samples. Analyte recoveries (75–105%), repeatability (RSDs 2–8%) and linearity (0.09–3.0 μg/l) were fully satisfactory.

An automated procedure consisting of LLE of 250 μl of urine at alkaline pH with 100 μl of methyl *tert*.-butyl ether, phase separation and split injection of 2 μl of the organic solvent has been developed for the determination of 34 basic and neutral drugs [103]. The Prepstation was used without further manual intervention to add an internal standard, a sodium hydroxide solution and the extraction solvent. Extraction yields of 27–102% (depending on polarity) were obtained which resulted in detection limits for most drugs of less than 0.5 mg/l. The method allows the preparation and analysis of the samples to be completely synchronised and showed good accuracy and precision.

Namera et al. [104] used a Prepstation for automated sample preparation combined at-line with GC–MS for the determination of seven barbiturates

in 1.5 ml of human urine. Sample enrichment and clean-up were performed on a disposable C_{18} cartridge and by washing with 2.5 ml of methanol–water (10:90, v/v). The barbiturates were eluted with 1.0 ml of chloroform–isopropanol (75:25, v/v) into an autosampler vial, and 1 μl was injected into the GC–MS system. Using an internal standard method, good linearity was obtained in the 0.02–10 mg/l range for all barbiturates.

It is interesting to contrast the mg/l performance of Refs. [103,104] with the μg/l results of [102], which is mainly the result of finally analysing a (minor) aliquot as against essentially the total sample.

In conclusion it can be said that much effort devoted to the development of on-line SPE–GC procedures and that the technique has become mature. Furthermore, all available detection devices for GC can be used as is briefly demonstrated in Table 2 which summarizes a selected number of applications for various analyte and sample types. The use of (tandem) MS and other spectroscopic detection methods (AED, FT-IR) merits special attention, because they provide structural information and, thus, enable provisional identification. All aqueous samples were analysed under real-life conditions. Detection in the ng/l range is seen to pose no problems.

4.3. SPETD–GC

An interesting approach for the injection of large volumes of aqueous samples into a GC system, which involves TD, was presented several years ago [105]. Up to 200 μl of an aqueous sample could be injected onto a Tenax-packed GC column at a temperature above the solvent boiling point, the water being eluted while the analytes were retained. With a two-oven system, the analytes were transferred in the split mode from the Tenax pre-column (in the first oven) to a capillary GC column (in the second oven) by heating the first oven with a steep temperature gradient.

The above concept was modified by using the packing material as in conventional SPE, i.e., via sorption in the liquid state, rather than injecting the water above the boiling point and adsorb analytes in the gaseous state [106,107]. Furthermore, the packed column was miniaturised in such a way that it could be placed in the liner of a PTV. After removal of the water by purging the packed bed in the liner with a carrier gas at a high flow-rate, the analytes were thermally desorbed by rapidly increasing the injector temperature and, subsequently, analysed by GC. Tenax sorbents were found to be best, but carbon phases also had suitable characteristics for use with SPETD, i.e., sufficient retention power for analytes in the liquid phase (during sorption) and good thermal stability (during desorption). The problem encountered with the carbon phases was the rather narrow application range, which is determined by loss of volatiles during drying on the ''volatile'', and by incomplete TD on the ''non-volatile'' end. The method was successfully tested with 10 μg/l stan-

Table 2
Selected applications of on-line SPE–GC procedures with various detection modes

Analytes	Sample type	Detection	LOD (ng/l)	Ref.
OCPs, PCBs	River water	ECD	1	[60,61]
Medium polar analytes	Water	FID	100	[63,64]
Steroid hormones	Urine	FID	100	[65]
Triazines	Waste water	NPD	10	[66]
	Orange juice			
Triazines, OPPs	River water	NPD	1–100	[55,68]
Triazines, OPPs, OSPs	River water	FPD	1–30	[69]
Atrazine, simazine	River water	SIM-MS	3	[73]
		Full-scan MS	30	
Various pesticides/herbicides	River/tap water	Full-scan MS	10–100	[71,76,90]
organic contaminants		SIM-MS	1–20	[82]
Various contaminants	River water	ITD–MS–MS	0.1–10	[81]
OPPS	River water	AED	2–5	[85]
PAHs, pesticides	River water	FT-IR	100–1000	[88,89]

dard solutions of *n*-alkanes and chlorinated benzenes and phenols. Typical results for six sorbents, which clearly show the different application ranges, are shown in Fig. 15.

A similar approach was used by Mol et al. [108] who studied the enrichment of environmental contaminants ranging in volatility from dimethylphenol to phenanthrene. Good results were obtained for sample volumes of up to at least 1 ml, as becomes evident from Fig. 16. When 250-μl samples spiked at 80 μg/l were used, recoveries were 65–100% and RSDs 1–13%.

In all of the above systems, elimination of water either caused problems or, at least, was time-con-

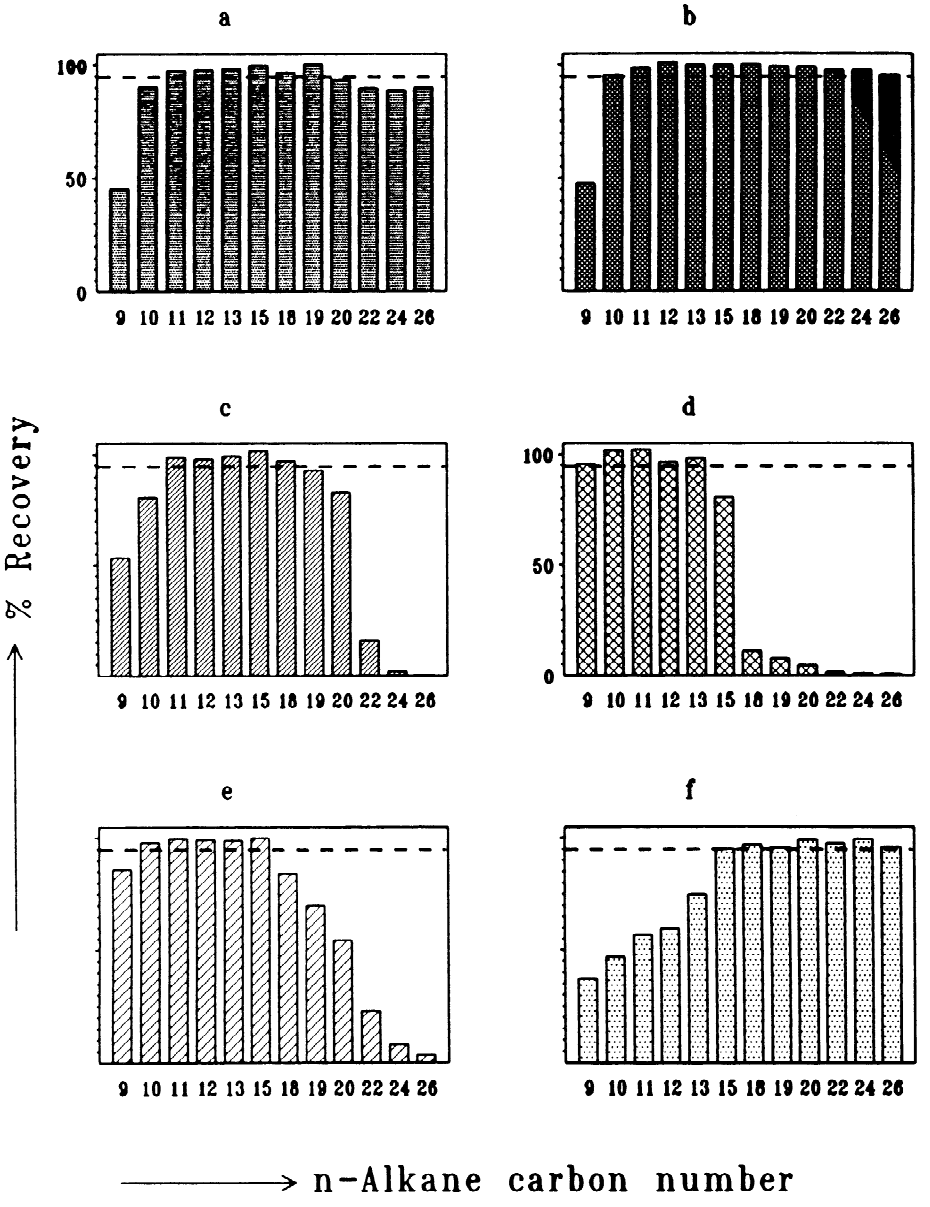

Fig. 15. Average per cent recovery ($n=3$) of *n*-alkanes after injection of 1 μl of *n*-alkane mixture, 10 min purging at 50°C using a high helium flow-rate, thermal desorption and GC–FID. Sorbents: (a) Tenax-TA, (b) Tenax-GR, (c) Carbotrap, (d) Carbopack B, (e) Hypercarb and (f) RP6-410 bonded silica [107].

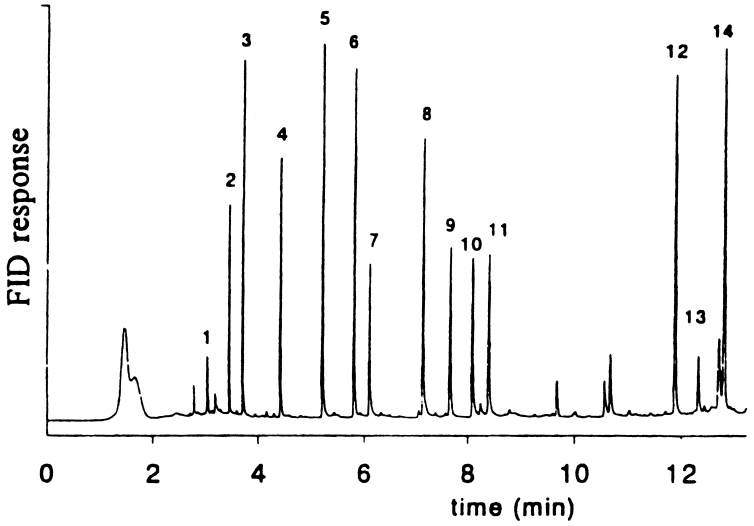

Fig. 16. SPETD–GC chromatogram of 1 ml water sample containing 10 μg/l of selected organic contaminants. Peak assignment: 1=toluene; 2=ethylbenzene; 3=methoxybenzene; 4=*p*-dichlorobenzene; 5=2,6-dimethylphenol; 6=2,6-dimethylaniline; 7=*p*-chloroanaline; 8=indole; 9=2,6-dichlorobenzonitrile; 10=2,4,5-trichlorophenol; 11=*p*-dinitrobenzene; 12=trifuralin; 13=atrazine; 14=phenanthrene. Introduction rate, 100 μl/min; PTV initial temperature, 30°C [108].

suming. Recently, an improved SPETD set-up was reported which was combined with FID and ITD tandem MS detection [109]. It includes a newly designed liner for a PTV, an improved water elimination step and washing with HPLC-grade water to prevent degradation of analytes due to interaction with remaining sample constituents. Detection limits of 0.1 μg/l were reported for alachlor and metolachlor when using sample volumes of only 100 μl. As an illustration, the presence of a suspected pesticide in harbour water was confirmed using EI and PCI in both the single- and tandem MS mode. Quantification gave a concentration of (1.2±0.1) μg/l with all four detection procedures.

A study using a set-up similar to SPETD, but with sorption onto the packing material in the liner taking place in the gaseous state, also revealed that Tenax materials were the best choice [110]. Due to the low evaporation rate of water (ca. 10 μl/min), injection took some 50 min. The evaporation process was investigated using a transparent ''injector'' [111], which resulted in suitable operating conditions for the injection temperature (50°C) and speed-controlled injection (10 μl/min). The system was used to determine several triazines in river water [112]. Frequent exchange of the insert was required to prevent discrimination of chemically labile substances caused by the deposition of salts and other matrix materials in the insert, and obtain satisfactory analytical data (recoveries, 80–104%; NPD limits, 0.01–0.02 μg/l for 500-μl injections).

Baltussen et al. recently introduced a modified version of the above concept [113]. On-line extraction of the analytes present in the water sample was carried out in a tube packed with pure polydimethylsiloxane (PDMS) particles. After drying of the packing, TD and transfer to the GC column were done via a PTV kept at sub-ambient temperature to ensure complete transfer of the enriched solutes. The whole system was automated and allowed the introduction of sample volumes of up to 10 ml. The authors claim that, compared with packing materials such as Tenax, PDMS offers the advantage of improved blanks although degradation products formed from the PDMS material were present in the chromatograms. As these degradation products contain a homologous series of siloxane breakdown products, they were easily identified by GC–MS and did not interfere with pesticides and polycyclic aromatic hydrocarbons (PAHs). However, the presence of the peaks is disturbing. A distinct advantage compared to the conventional set-up of SPETD is

that the sampling tube can have a length of up to 25 cm, which allows larger sample volumes to be analysed with corresponding increase in analyte detectability. A disadvantage when comparing the technique with SPE–GC procedures appears to be the long time required for conditioning, sampling and clean-up (each step of 10 ml takes 30 min).

A theoretical model was derived which allowed calculation of breakthrough volumes from octanol–water partitioning coefficients (K_{ow}). For a sample volume of 10 ml, theory predicted that a log K_{ow} of 1.8 was required for quantitative recovery. As is commonly seen in on-line equipment, for the most apolar solutes, with a log K_{ow} higher than 7, low recoveries were found due to adsorption to tubing and valves in the system. The procedure gave detection limits in the order of 10 ng/l using MS detection in the full-scan mode.

4.4. OTT–GC

An alternative to trapping analytes by SPE is trapping them in the coating of a short piece of a capillary GC column. Although several attempts have been made to couple an open-tubular trap (OTT) with capillary GC [114–116], only the studies by Mol et al. have led to an on-line method [117]. In their system the analytes present in the aqueous sample were trapped on a 2 m×0.32 mm I.D. OTT coated with a 5-μm thick stationary phase, water being removed by a slow flow of nitrogen. Desorption was carried out with an organic solvent and transfer to the GC system was done using a PTV injector as interface [118].

One can derive that breakthrough of an analyte will occur when [119]:

$$V_b = K_D V_s \left(1 - 0.9\sqrt{\frac{F}{D_m L}}\right) \quad (3)$$

where V_b is the breakthrough volume and K_D the distribution constant of the analyte, V_s the volume of the stationary phase, F the flow-rate of the aqueous sample, D_m the diffusion coefficient of the analyte in water, and L the length of the trap. Obviously, the flow-rate should not exceed a certain threshold value or breakthrough will occur immediately. In actual practice the maximum flow-rate that can be used is ca. 0.2 ml/min for a 2 m×0.32 mm I.D. OTT. On the other hand, the use of a thick-film stationary phase will increase the breakthrough volume. More recently it was demonstrated that for coiled or stitched columns much higher sample flow-rates, i.e., up to 4 ml/min, are allowed [120] because, in deformed capillaries, a secondary flow is induced which enhances radial dispersion.

An interesting way to increase the values of K_D and V_s, and, thus, of V_b, is to use an organic desorption solvent which also causes substantial swelling of the stationary phase. It should, however, be realized that water should not dissolve in the organic solvent, nor should the organic solvent dissolve in water. In the former case, water would be injected into the GC system, while in the latter case the swollen stationary phase would lose (part of) the swelling agent. Finally, the organic solvent should smoothly evaporate during analyte transfer.

As an illustration of the above, Table 3 shows the gain in breakthrough volume that can typically be obtained when the stationary phase of the OTT is swollen before analyte trapping. Without swelling only apolar compounds such as phenanthrene and trifluoralin are well retained. When using an alkane such as *n*-pentane all apolar compounds show good retention, while more polar solvents, such as chloroform, give better results for more polar analytes.

The OTT–GC–FID system was used to determine the test compounds of Table 2 in river water, urine and serum samples. In all cases analyte recoveries were satisfactory with RSD values for the total analysis of 1–10%. Fig. 17 shows the analysis of river water spiked at the 5 μg/l level [117]. Detection limits are in the ng/l to μg/l range depending on the amount of sample taken and the FID response of the test analyte.

4.5. SPME–GC

SPME is an extraction technique which has made much progress in the recent past. SPME can be combined at-line with GC, and automated using a modified autosampler [121–123]. Analytes are extracted by a small-diameter fused-silica fibre that is coated with a polymeric phase which is immersed in the sample container. The analytes partition into the stationary phase until plateau conditions have been

Table 3
Breakthrough volumes for a selected number of analytes in OTT–GC using a 2 m×0.32 mm I.D., 5-μm thick trap without and with swelling

Analyte	Breakthrough volume (ml) with swelling agent				
	None	*n*-Pentane	Dichloromethane	Chloroform	Isopropylchloride
Toluene	0.5	>10	2	5	>10
Ethylbenzene	1	>10	2.5	5	>10
Methoxybenzene	<0.5	2.5	1.5	5	5
Dichlorobenzene	<0.5	>10	2.5	5	>10
Dimethylphenol	<0.5	<0.5	1	2.5	1
Dimethylaniline	<0.5	<0.5	1.5	5	1.5
Chloroaniline	<0.5	<0.5	1	2.5	1
Indole	<0.5	<0.5	1.5	2.5	1.5
Dichlorobenzonitrile	<0.5	2.5	1.5	5	10
Trichlorophenol	<0.5	1	1.5	5	5
Dinitrobenzene	<0.5	<0.5	1.5	5	2.5
Trifluralin	>10	>10	>10	>10	>10
Atrazine	<0.5	<0.5	2.5	2.5	1.5
Phenanthrene	>10	>10	>10	>10	>10

reached, which typically takes 2–60 min (with the higher values for higher-molecular-mass analytes), and can be aided by sample agitation via a stirring bar or vibration.

An SPME unit consists of a coated fibre bonded onto a stainless steel plunger and a holder which looks like a modified syringe. By using the plunger, the fibre can be drawn into the septum-piercing needle for protection. The needle also provides protection during GC injection. After injection, the adsorbed analytes are thermally desorbed, cryofocused and analysed by GC. TD should be carried out at a temperature above the boiling point of the least volatile analyte of interest. The cryofocusing step is required because desorption may take quite some time, i.e., on the order of a minute. Accuracy can be influenced by the time elapsing between sorption and desorption (loss of volatiles). Further, the position of the fibre in the injector is important, because of a temperature gradient in the injector. Another critical point is that the volumes of samples and standards should be the same during analysis by SPME.

One should realize that in SPME the extraction process reaches an equilibrium and is, in most instances, not exhaustive at all, as is almost invariably the case in SPE. The amount of analyte that will be extracted can be calculated from:

$$n_s = K_D V_s C_{aq} \quad (4)$$

where n_s is the number of moles of analyte sorbed in the stationary phase, K_D the distribution constant of the analyte, V_s the volume of the stationary phase, and C_{aq} the analyte concentration in the aqueous sample. Obviously, repeated injection from the same sample will not give accurate results for compounds with high distribution constants, since these compounds become more or less depleted even after one extraction. However, for compounds with relatively small K_D values, this problem will not occur – though at the cost of a serious loss of analyte detectability. Recently, a book on SPME and a well-documented reviews appeared, and the reader should consult the quoted literature for other experimentally important aspects (extraction time, stirring rate, ion strength, pH, temperature, modifier addition) [123–126].

Extraction of volatile or semi-volatile analytes present in aqueous or solid samples can also be performed from the headspace, if necessary after heating the sample to enhance migration of the analytes into the gas phase, with similar detection limits as reported for conventional SPME [127–136]. Extraction kinetics in headspace analysis are dependent on the headspace capacity [137]. If it is sufficiently large, the analytes are extracted almost exclusively from the gaseous phase, and equilibration can be very fast (within 1–1.5 min). On the

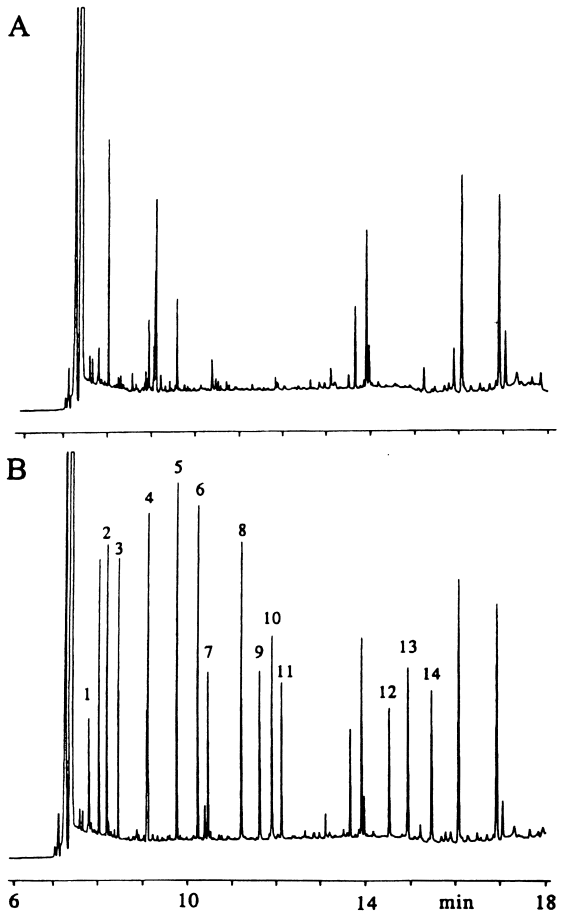

Fig. 17. On-line OTT–GC–FID of 2.25 ml River Dommel water (a) without and (b) with spiking at the 5 μg/l level. Peak assignment as in Fig. 16 [117].

other hand, a large headspace volume causes a significant loss of sensitivity.

4.5.1. Fibres

Initial investigations were carried out using a PDMS-coated fibre, which showed good analytical performance for apolar analytes of low molecular mass and volatiles [121]. This phase is commercially available in various thicknesses [122]. Extraction of more polar analytes requires more hydrophilic phases. Analytes such as phenols are preferably extracted with a polyacrylate coating [138,139]. Analytes for which PDMS fibres give a low recovery or even none at all, copolymers containing divinylbenzene (DVB), such as Carbowax–DVB and PDMS–DVB can be used. The former coating was used to extract barbiturates from urine samples [140], and the latter to determine alcohols in whole blood and urine using the headspace approach [128]. It has to be added, however, that stronger fibre/analyte interactions which promote extraction, play an adverse role during TD. In the case of the barbiturates, phenobarbital was not quantitatively desorbed even after 6 min exposure at 250°C. The PDMS–DVB fibre was used for the analysis of chemical warfare agents in natural waters with good recoveries and sub-μg/l level detection limits (detection: NPD or SIM-MS) [141].

In recent studies coatings containing carbon are used. Two new phases are Carboxen–PDMS [135] and graphitized carbon black [142]. Since interaction between analyte and carbon is rather strong, these fibres have been tested for the enrichment of volatile organic compounds from water and air. Detection limits at the low ng/l level are possible when selective detection is used after GC separation, e.g., ECD for halocarbons and SIM-MS for other volatile compounds. The Carboxen–PDMS fibre shows better extraction efficiency than a 100-μm PDMS fibre and similar fibres, but repeatability was poorer and equilibrium more time-consuming. Distribution coefficients of the BTEX compounds between an aqueous solution and the Carboxen–PDMS fibre were calculated and compared with the results of other researchers and with octanol–water partition coefficients.

4.5.2. Derivatization–SPME–GC

In most studies on derivatization combined with SPME, the reaction takes place in the aqueous phase. The apolar products are more amenable to the SPME process and the higher recoveries result in lower detection limits. Chlorinated acetic acids were derivatized in situ to their methyl esters using HCl and methanol, and determined by GC–ECD with detection limits at the low μg/l level [143]. Pentafluorobenzyl bromide and (pentafluorophenyl) diazoethane were used to derivatize short-chain fatty acids directly in sample matrices for sensitive ECD [144]. Primary amines were derivatized with pentafluorobenzylaldehyde [145]. Ionic organometallic species could be separated after alkylation with

tetraethylborate under alkaline conditions. Mercury-, lead- and tin-containing compounds were derivatized in situ with sodium tetraethylborate [130], while arsenic compounds were derivatized with 1,3-propanedithiol or 1,2-ethanedithiol [146] sorbed on a fused-silica fibre, and desorbed in the splitless injection port of the GC system. GC with inductively coupled plasma (ICP) MS detection resulted in detection limits of 0.3–2 ng/l (as Sn) for monobutyl-, dibutyl- and tributyltin [130].

SPME of various metabolites of naphthalene, phenanthrene and pyrene was performed by headspace silylation with *N,O*-bis(trimethylsilyl)trifluoroacetamide without any catalyst for on-fibre derivatization and GC–MS in the single-ion recording mode. The method was used for the profile analysis of PAH metabolites in smoker's urine after enzymatic cleavage; there were no interferences due to matrix peaks.

Chemical derivatization with *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine hydrochloride of 23 carbonyl compounds in water resulted in products with high ECD responses. SPME took place in the liquid or the headspace. The RSDs for the determination of the carbonyl compounds in distilled water, ozonated drinking water, and rain water were 6–21% (no internal standard). With 4 ml of sample, the LODs for most compounds were 0.006–0.2 μg/l, except for glyoxal and methylglyoxal which showed low sensitivity in headspace SPME.

A technique that is only possible in combination with SPME is on-fibre derivatization. Analytes are chemically converted after extraction (either from the water or the head space) by applying the reagent as gas. A prerequisite is that the analytes can be extracted, which means that (very) polar analytes cannot be handled. Furthermore, no chemical reaction should occur with the fibre. Diazomethane and pyrenyldiazomethane were the first reagents described [144] for effective on-fibre derivatization of long-chain and short-chain fatty acids, respectively, to increase their detectability.

4.5.3. Other applications

Several interesting applications of SPME–GC have been reported. The majority of these deal with rather volatile analytes such as the BTEX mixture and other substituted benzenes [138,139,147–154] and with a variety of pesticides [155–166]. Fig. 18 shows the SPME–GC–MS chromatogram of the OPPs diazinon, fenitrothion and isoxathion in Lake Ontario water [163]. Analytically relevant data on a number of applications are compiled in Table 4. It has to be added that analyte recoveries are rarely reported in SPME.

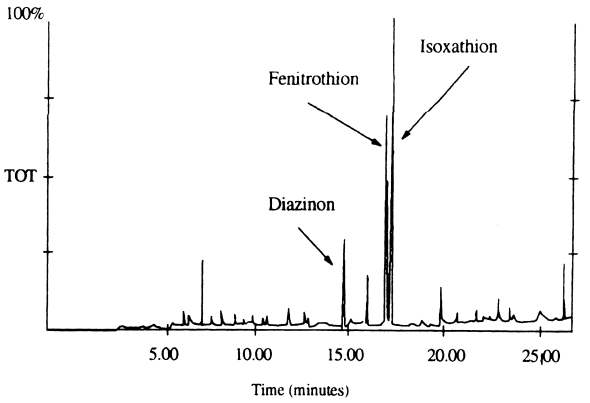

Fig. 18. SPME–GC–MS chromatogram of Lake Ontario sample spiked with diazinon, fenitrothion and isoxathion [163].

The extraction efficiency of polar analytes will be rather, or even very, low because of the relatively small K_D values. Recently, results of an interlaboratory test on the determination of semi-volatile pesticides were reported [165]. The test proved that SPME is an accurate sample preparation procedure, and can be used for screening as well as quantitative analysis.

5. Conclusions

Despite some encouraging developments, on-line RPLC–GC with its partly aqueous LC eluents and aqueous samples has not become a successful technique [174]. An early breakthrough requires further investigations of, e.g., the vaporizer chamber/precolumn solvent split/gas discharge interface [2] or water-resisting retention gaps [29]. Its counterpart, on-line SPE–GC, is a technique with which analytes are isolated/extracted from an aqueous sample and, next, on-line desorbed and transferred to the GC part of the system, and analysed. Elegant solutions to most practical problems have been reported. Water

Table 4
Summary of applications of SPME of aqueous samples

Analyte	Matrix	Detection	LOD	Ref.
BTEX	Ground water	ITD	30–80 ng/l	[147]
Substituted benzenes	Ground water	FID	1–3 μg	[149]
	Water	MS	1–10 ng/l	[148]
Volatile hydrocarbons	Water	ECD	1–130 ng/l	[150]
	Drinking water	ITD	20–200 ng/l	[152]
Phenols	Ground water	ITD	5 μg/l	[138]
	Sewage water	ITD	0.01–1.6 μg/l	[139]
N-herbicides	Water	NPD	0.01–6 ng/l	[156]
		MS	0.01–6 ng/l	
N-pesticides, OPPs	Water	MS	5–90 ng/l	[157]
Cl-pesticides	Ground water	NPD	5–90 ng/l	[158]
	Lake water	ECD	0.05–1.6 μg/l	[146]
Metolachlor	Tile drainage water	ECD	2 ng/l	[162]
OPPs	Water	NPD	0.009–0.5 μg/l	[163]
N/Cl-pesticides, OPPs	Water	MS	1–60 ng/l	[164]
Parathion, malathion	Water	FID	0.5 μg/l	[166]
Methadone	Urine	MS	20 μg/l	[167]
EPA 624	Water	ITD	1–5 μg/l	[168]
Organic pollutants	Water	ECD	0.05–1.6 μg/l	[169]
PAHs, PCBs	Waste water	ITD	1–20 ng/l	[170]
Fatty acids	Sewage water	FID	0.02–760 μg/l	[171]
Microcontaminants	Water	FID	0.2–5 μg/l	[172]
Fuel hydrocarbons	Waste water	FID/MS	0.03–1 μg/l	[173]

can be removed by means of a nitrogen purge or an on-line inserted drying cartridge. An alternative is the direct introduction of water utilizing a water-resistant retention gap. The use of a nitrogen purge is the most straightforward and easy-to-use technique. Removal of traces of water with an on-line drying cartridge is less time-consuming but the adsorption of polar analytes to the packing of the cartridge is a cause of some concern. It is encouraging to note that all three approaches have been used successfully for surface and drinking water studies, and have been combined with a variety of selective GC detectors and, increasingly, with MS detectors. It is justified to state that automated SPE–GC-based water analysis is now available for routine operation.

For those who are not yet convinced that LC-type SPE operations can be combined on-line with GC to provide integrated analytical systems, there are other options, such as LLE–GC which may well be highly useful for monitoring waste water and other such flowing sample streams, and techniques which involve thermal rather than solvent desorption (SPETD–GC and SPME–GC) which will probably be especially attractive when relatively volatile solutes are of interest. Today, SPME–GC is already being used by many workers and many applications have been reported. In addition, next to on-line analyte isolation–GC techniques, the at-line combination of automated extraction and LVI–GC, which has recently been described for a Prepstation–GC combination, may well become of distinct interest.

Next to selecting the proper on-line analyte isolation–GC procedure, combining this procedure with a suitable detector is of vital importance. Until quite recently, selective GC detection methods such as NPD, FPD or ECD, were used in the vast majority of all studies. However, in recent years, hyphenation has become increasingly important. Of course, GC–MS already has a long and successful history, but its widespread use for routine applications is relatively novel. With the advent of the ion-trap detector, tandem MS has become an additional, and distinctly attractive, option. Since analyte identification/confirmation is becoming increasingly important in many areas, and especially in environmental chemistry, there is little doubt that the use of MS detection will continue to increase. AED and FT-IR detection should also be mentioned. In the past few years

GC–AED has been shown to be user friendly and to provide information which is often complementary to that of GC–MS procedures. The excellent element selectivity makes the AED especially useful for general screening purposes and several interesting studies on SPE–GC–AED and SPE–GC–AED–MS have been reported. Also the progress so far in the area of FT-IR detection, has led to an on-line system using a sample storage interface, i.e., direct deposition or cryofocusing (which provides much better sensitivity than a lightpipe detector) can be achieved, and concentration detection limits of 0.1–1 μg/l have been reported for various pesticides. There is no doubt that the possibility of analyte recognition at the trace level by means of FT-IR detection, will be regarded a highly welcome addition to the list of identification techniques for GC.

Finally, it seems safe to state that on-line SPE–GC and SPETD–GC, and also some of the other techniques discussed above, enable quantitative analyte isolation (and separation) from aqueous samples of up to 10–100 ml. On the other hand, with many of the detectors referred to, detection limits will at least be as good as 1 ng and, in many instances, 10–100 pg. Table 5 clearly demonstrates the cumulative effect of a combination of on-line sample preparation and sophisticated detection in a GC-based analytical procedure. Even with very modest detection performance, a 10-ml sample is all that is required to reach the 0.1 μg/l detection limit of the European Union (EU) drinking water directive. If analyte detectability is good (but, certainly, not exceptionally so), sample volume can be reduced to 0.1 ml or, alternatively, the sample volume of 10 ml can be maintained and the detection limits improved to about 1 ng/l. Examples of both options can be found in the literature, e.g., in Refs. [81,109]. No doubt, with the technical progress to be expected for the next few years in mind, one can confidently state that an increasing number of real-world applications will be reported which will share the advantages of rather small sample volumes, high sample throughput, and neglible consumption of organic solvents.

Table 5
Estimated detection limits (μg/l) for an on-line analyte isolation–GC–detection system

Sample volume (ml)	Detection limits (μg/l) for absolute detector sensitivity of:		
	10 pg	100 pg	1 ng
0.1	0.1	1	10
1	0.01	0.1	1
10	0.001	0.01	0.1

Finally, even for those who agree that the above discussions and conclusions are correct, but themselves have to deal with analytical procedures with which sample preparation and separation-plus-detection cannot be combined on-line, there is good news. Scrutiny of the recent literature reveals that elution of SPE cartridges typically used in SPE–GC, does not require more than 500 μl of organic solvent, and often distinctly less. Since LVI of about 100 μl can be performed without any problem, at least 20% of the extract can be injected. Or, in other words, if the sample volumes of Table 5 are increased from 0.1–10 ml to 0.5–50 ml, the same performance can be obtained as calculated there at what can be said to be little additional cost or run time.

6. Glossary

AED	Atomic emission detection
ASPEC	Automated sample preparation with extraction columns
BTEX	Benzene, toluene, ethylbenzene and xylenes
CI	Chemical ionization
DVB	Divinylbenzene
ECD	Electron-capture detection
EI	Electron impact ionization
FCSE	Fully concurrent solvent evaporation
FID	Flame ionization detection
FPD	Flame photometric detection
FS	Full scan
FT-IR	Fourier transform infrared
GC	Gas chromatography
HCH	Hexachlorocyclohexane
ICP	Inductively coupled plasma
ITD	Ion trap detection
LC	Column liquid chromatography
LLE	Liquid–liquid extraction
LOD	Limit of detection
LVI	Large-volume injection

MS	Mass spectrometry
MID	Multiple ion detection
NCI	Negative chemical ionization
NP	Normal-phase
NPD	Nitrogen–phosphorus detection
OPP	Organophosphorus pesticide
OTT	Open-tubular trap
PAH	Polycyclic aromatic hydrocarbon
PB	Particle beam
PCB	Polychlorinated biphenyl
PCI	Positive chemical ionization
PCSE	Partially concurrent solvent evaporation
PDMS	Polydimethylsiloxane
PROSPEKT	Programmable On-Line Solid-Phase e(k)xtraction Technique
PTV	Programmed-temperature vaporizer
RP	Reversed-phase
RSD	Relative standard deviation
SIM	Selective ion monitoring
SPE	Solid-phase extraction
SPETD	Solid-phase extraction–thermal desorption
SPME	Solid-phase microextraction
SVE	Solvent vapor exit
TD	Thermal desorption
TIC	Total ion current

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